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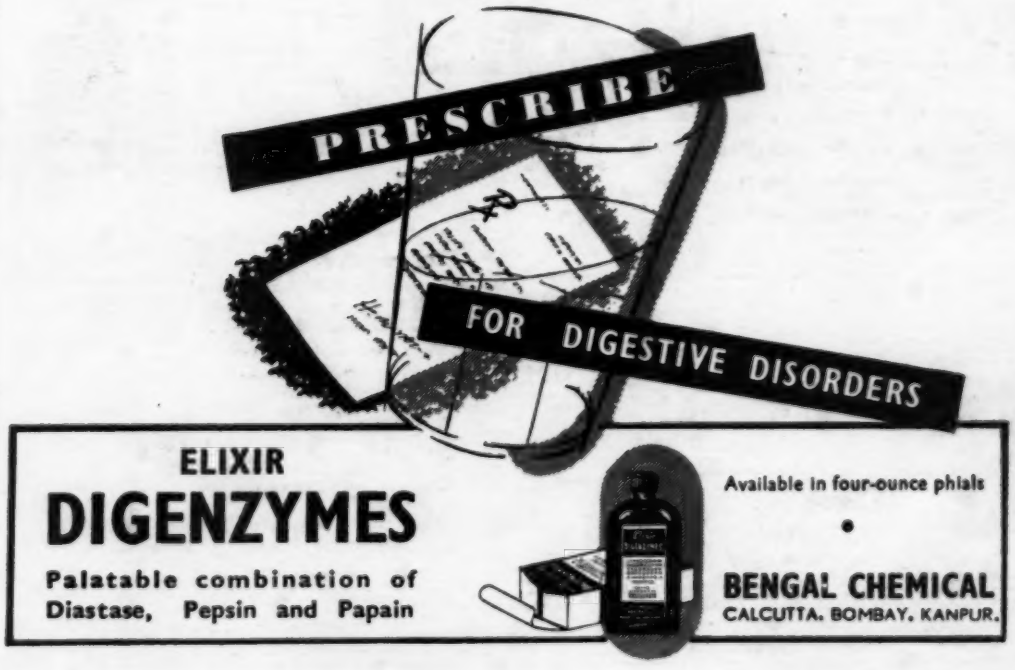

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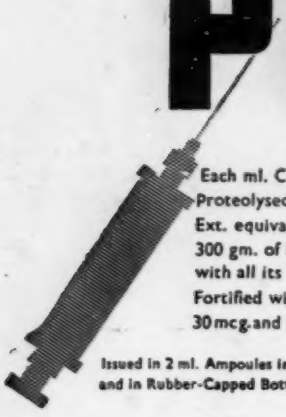

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TABLE OF CONTENTS

ORIGINAL ARTICLES:

1. Cerebral Thrombosis—M. Hanumantha Rao 529
2. Observations on Acquired Aplastic Anaemia —J. B. Chatterjea, Sushiela Swarup, S. K. Ghosh and D. K. Banerjee 536
3. Mitral Stenosis without Diastolic Murmur —G. C. Sepaha, S. R. Jain and C. R. Bhandari 543
4. A Study on Coronary Vascular System —S. K. Chatterjee 547

SPECIAL ARTICLE:

New Oral Hypoglycaemic Agents in Non-hormonal Therapy of Diabetes Mellitus—B. J. Mehta and G. J. Kothari 549

CASE NOTES:

1. Chorionepithelioma with Unusual Features— S. Hazra and S. K. Paul 557
2. Normalisation of Carbohydrate Metabolism in Maturity Onset Type of Diabetes—S. K. Mukherjee and S. S. Mukherjee 560

EDITORIAL:

Polypeptides Affecting Smooth Muscles and Blood Vessels 562

PRESIDENT'S PAGE:

1. Address at the Niiratan Sircar Centenary Celebrations 564
2. Inaugural Address at the Silver Jubilee Celebrations of Barrackpore Branch, I.M.A. 565

GENERAL PRACTICE DIGEST 566

CURRENT MEDICAL LITERATURE 568

NOTES AND NEWS 570

CORRESPONDENCE 575

REVIEWS 576

OBITUARY 578

YOUR QUESTIONS 578

SUPPLEMENT:

1. XXXVII All India Medical Conference, Kanpur, January 4-6, 1962 579
2. Branch Notes 580

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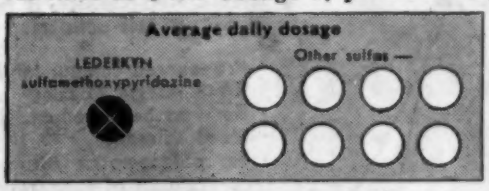

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Index to Advertisers

	Page
Adcco Ltd.	xliv
Alembic Chemical Works Co. Ltd.	xxx, xxxi, xxxv
Allen & Hanburys Ltd.	xii
Antiseptic	xiii
Atul Drug House	x
Bengal Chemical & Pharm. Works Ltd.	Front Cover
Bengal Immunity Co. Ltd.	2nd Cover
Boehringer-Knoll Ltd.	ix
Boots Pure Drug Co. (I) Pvt. Ltd.	xiv
Brahmachari Research Institute	xlviii
Comteck Laboratories	xx
Decruz Corporation	xlvi
Dey's Medical Stores Pvt. Ltd.	xvii
Eastern Drug Co. Ltd.	iv
East India Pharm. Works Ltd.	xxviii
Franco-Indian Pharm. Pvt. Ltd.	vii, xi, xix
G. D. Pharmaceutical Pvt. Ltd.	xx
Glaxo Laboratories (I) Pvt. Ltd.	xliii
Himalaya Drug Co.	xxxviii
Hind Chemicals Ltd.	xxii
Hoechst Pharm. Ltd.	xxix, xxxvi
Indian Health Institute & Lab. Ltd.	xxiv
International Chemical & Biological Institute Pvt. Ltd.	xxxviii
J. J. DeChane	xvi
Johnson & Johnson of India Ltd.	xxxiii
John Wyeth & Brother Ltd.	xxxii
Kaira District Co-operative Milk Producers' Union Ltd.	xviii
Kemp & Co. Ltd.	xiii
Khandelwal Laboratories Pvt. Ltd.	ii, xv, xxvii
Khatau Valabhdas & Co.	xxi
Lederle Laboratories (I) Pvt. Ltd.	i
May & Baker (I) Pvt. Ltd.	x, 3rd Cover
Metrimpex (Hungarian Trading Co.)	iii
Mysore Industrial & Testing Lab. Ltd.	3rd Cover
Navaratna Pharm. Laboratories	xxiv
Neo-Pharma Pvt. Ltd.	v
Oriental Pharm. Industries Ltd.	xlviii
Parke Davis (I) Ltd.	xxxiv
Phoenix Drug House Pvt. Ltd. (Fairfield Syndicate Agency Pvt. Ltd.)	xliv
Rallis India Ltd.	xi
Ranbaxy & Co. Pvt. Ltd.	xxvi
Raptakos, Brett & Co. Pvt. Ltd.	xxvi
Retort Laboratories	3rd Cover
Roche Products Ltd. (Voltas Ltd.)	xxxix
Sarabhai Chemicals	xxiii
Sarabhai Merck Ltd.	xiv
Scientific Publication Concern	xlvi
Smith, Kline & French (I) Ltd.	viii, xiii, xxv
Smith Stanistreet & Co. Ltd.	xlvii
Stadmed Pvt. Ltd.	xxii
Standard Pharm. Works Ltd.	vi
Suhrid Geigy Trading Ltd.	xxxvii
Unichem Laboratories	Back Cover
Uni-U.C.B. (I) Pvt. Ltd.	xlvi
Veb Carl Zeiss Jena	xxiv
Warner-Lambert Pharm. Co.	xii
Yoga-Mimansa Lab.	3rd Cover
Zandu Pharm. Works Ltd.	vi

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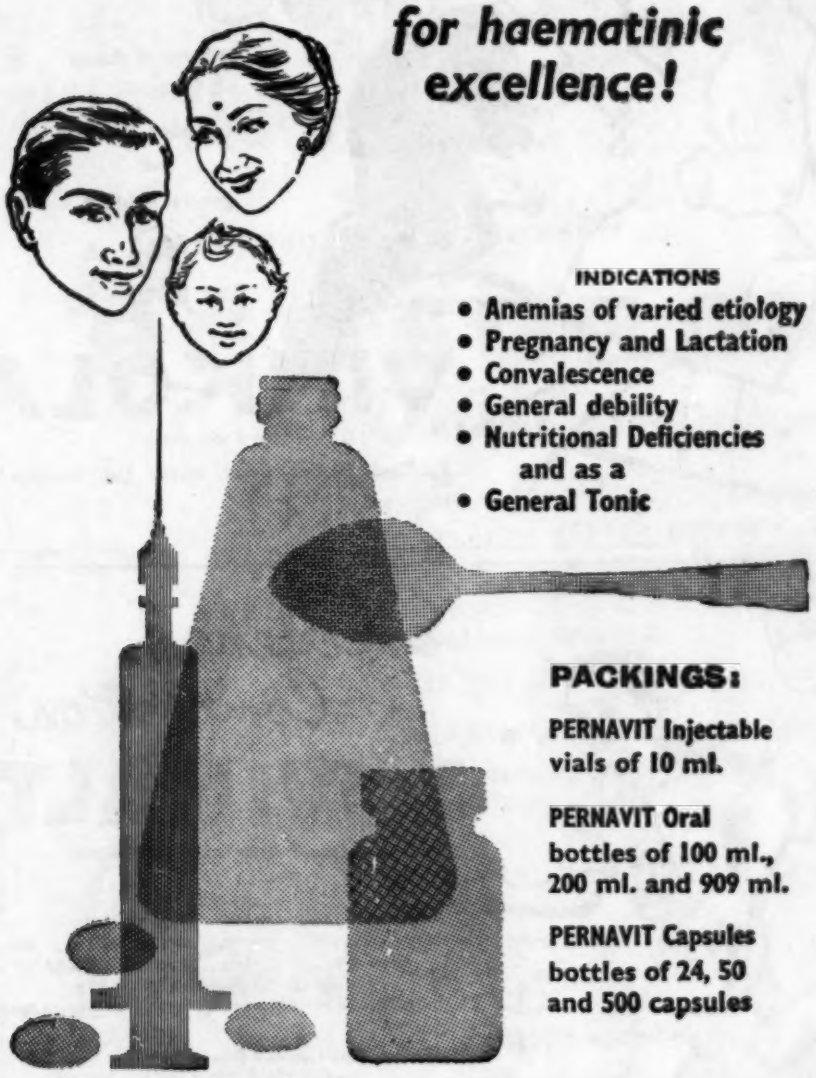

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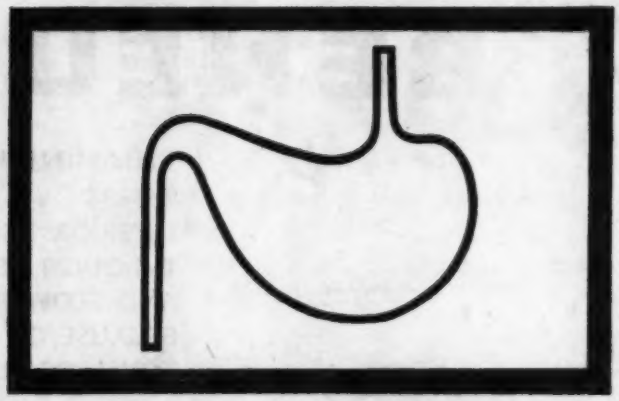

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* *Food Science* 6 (10) 241
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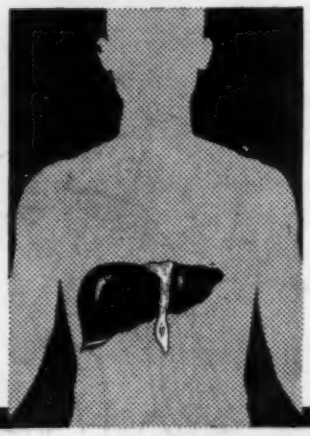

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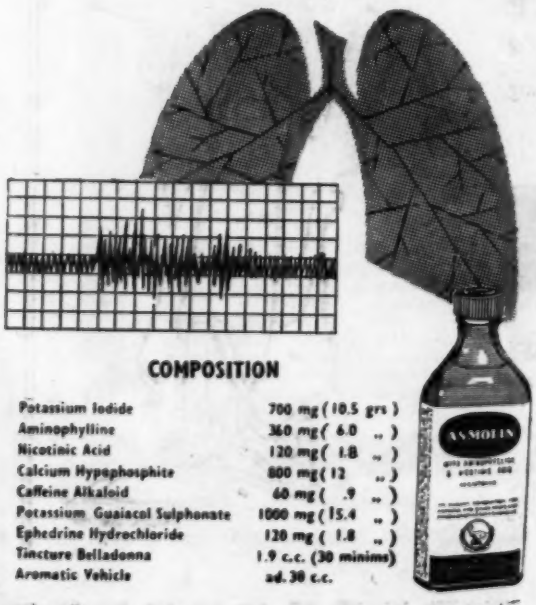

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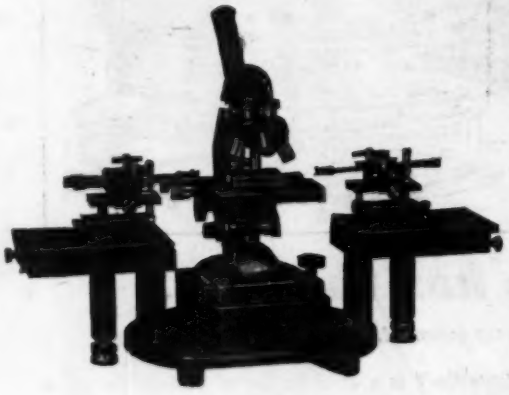

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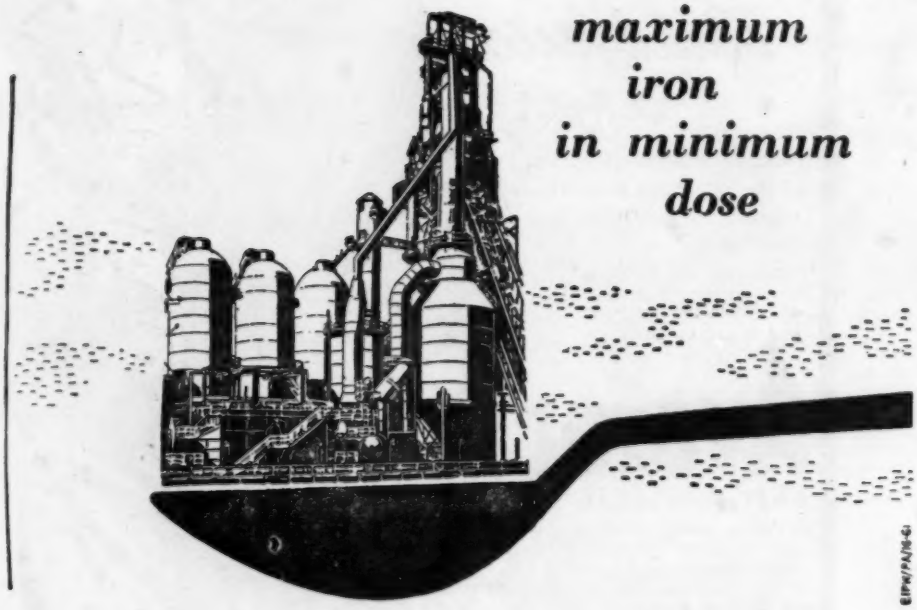

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ORIGINAL ARTICLES

CEREBRAL THROMBOSIS*

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Assistant Professor of Medicine, Osmania Medical College, Hyderabad

Cerebrovascular disease is of growing concern to the general practitioner, internist, geriatrician as well as to the neurologist and the neurosurgeon. Disorders of the intracranial circulation constitute the paramount problem in clinical neurology today. The number of patients with cerebrovascular accidents admitted is much more than any other type of disorder of the nervous system. It has been estimated that major brain stroke is the third most frequent cause of death in U.S.A., outranked only by heart disease and malignancy. The progressive aging of the population is largely responsible for the increasing incidence of cerebrovascular accidents.

A great deal of work has been done on the cerebral circulation and its regulation. The increase in the average age of the population makes the study of circulation of great importance to the practising physician who needs to know what bearing these studies have on the management of the increasing number of elderly patients. The introduction and extensive application of diagnostic techniques particularly percutaneous angiography is revealing more and more cases of vaguely classified neurologic syndromes, especially in the young, to be of cerebrovascular origin.

The present study of cerebrovascular lesions was confined to those of thrombosis only for the following reasons:

1. Haemorrhage was almost always fatal in a few days and did not lend itself for investigations and study.
2. The incidence of embolism in the wards was rare.

The aims of the study were:

1. To assess the incidence of cerebral thrombosis in the Osmania General Hospital, Hyderabad.
2. To study the clinical features of cerebral thrombosis with special reference to carotid artery thrombosis.
3. To find out the aetiology of cerebral thrombosis.

INCIDENCE

The incidence of cerebrovascular diseases admitted into the Osmania General Hospital, during the years 1954-58 is given below. The data have been analysed with a view to study the aetiological factors and the clinical features to the extent the records made possible.

1. The total number of cases of cerebral thrombosis admitted during the period is 604.

The total number of cases of cerebrovascular diseases admitted during the same period is 872.

The *incidence of cerebral thrombosis* is 69·2 per cent. of cerebrovascular disorders (Table 1).

2. *Sex incidence*—The sex incidence is: Males 319 (52·9 per cent.), females 285 (47·1 per cent.).

3. *Age incidence of thrombosis*—It would be observed from Table 1 that the maximum incidence of thrombosis occurred in the age group of 41 to 60 years (40·4 per cent.) and the next highest incidence occurred in the age group of 20

* Based on the dissertation accepted for the M.D. degree of the Osmania University, Hyderabad.

TABLE 1—SHOWING COMPARATIVE AGE INCIDENCE AND MORTALITY RATE IN OSMANIA GENERAL HOSPITAL SERIES AND MERRIT'S SERIES

Age group	Incidence			Mortality rate	
	O.G.H. series		Merrit's series	O.G.H. series	
	No.	%	%	No.	%
Under 20	16	2·6	—	—	—
20 — 40	192	31·7	1	—	—
41 — 60	244	40·4	31	46	62·1
61 — 80	143	23·6	61	24	32·5
Over 80	9	1·7	7	4	5·4

to 40 years (31·7 per cent.) in the Osmania Hospital series. The corresponding figures of incidence in Merrit's (1955) series are 61 per cent. in the age group of 61 to 80 and 31 per cent. in the age group of 41 to 60 years. This difference in the highest incidence in the age groups in our series and those of Merrit's series could be explained by the increased longevity and the care of the geriatric patients in U.S.A. compared to what obtained in this country.

The mortality rate of patients with thrombosis in our series is highest in the 41 to 60 age group (62·1 per cent.), when the incidence also is the highest, and the next highest age group of 61 to 80 has a mortality rate of 32·5 per cent.

4. *Incidence of aetiological factors*—The following is the incidence of aetiological factors of cerebral thrombosis cases in the Osmania General Hospital series (Table 2).

TABLE 2—SHOWING INCIDENCE OF AETIOLOGICAL FACTORS

Diseases	No. of cases	Percentage
Hypertension with atherosclerosis	204	33·7
Atherosclerosis with normal B.P.	281	45·7
Syphilis	96	15·8
Hypertension plus syphilis ...	18	2·9
Puerperal sepsis	23	3·8

Vakil (1951) in a statistical analysis of 1860 cases of cerebrovascular diseases associated with heart disease has noted an incidence of 148 cases, giving an incidence of 8 per cent. The incidence of thrombosis in his series was 61 per cent.

5. *History of previous episodes*—A history of previous episodes of cerebrovascular insufficiency or thrombosis was found only in 37 cases of the present series of 604 cases. The history was negative in 258 cases and was not elicited in the remaining ones.

CASE REPORTS

Case 1—R., male, aged 35, labourer by occupation, resident of Hyderabad was admitted on 24-12-1957 with history of unconsciousness of one day's duration. The attack of unconsciousness was preceded by an attack of gastro-enteritis two days prior to admission. Clinical examination revealed that he was semi-conscious, with response to deep stimuli present. There were also signs of dehydration. There was hemiplegia on the right side of the body including the face. Fundoscopy showed that the margins of the left optic disc were indistinct, the optic disc was swollen, the vessels were narrowed, with widespread haemorrhages along the vessels. The carotid pulsation on the left side of the neck was feeble. B.P. was 135/80 mm. Hg. Heart and lungs were normal. Blood W.R. was negative. Open angiography was done on the left side which showed a thickening of the carotid artery with feeble pulsations. The left internal carotid system was not filled, but only the external carotid and its branches were filled (Fig. 1, *vide* Plate). The patient was treated on symptomatic lines—the dehydration was corrected, and he made a good recovery.

Case 2—S., male, aged 29, clerk, resident of Secunderabad, was admitted on 13-1-1958 with history of difficulty in speech of one year's duration. In December 1956 he was treated for aphasia and right hemiplegia for about a fortnight in the K. E. M. Hospital and made a good recovery of the power, but the difficulty in speech persisted. Examination revealed dysphasia of the expressive type. Patient was a right-handed person without any defect in hearing or in sight. There was slight weakness of power in the right upper limb. The carotid pulsation was not felt on the left side. The other systems were normal. B.P. was 124/90 mm. Hg. Blood W.R. was negative. An open angiogram was taken on the left side. The artery was found to be thickened and unhealthy. The pulsation was feeble. Angiography showed an almost complete block of the common carotid at the level of its bifurcation.

Case 3—P., female, aged 30, was admitted on 12-8-1958 with diminution of vision and diplopia in the left eye of one year's duration and weakness in the right half of the body of 15 days' duration. Speech was normal. Patient was a right-handed individual. Examination revealed diminished vision in the left eye (6/20), right homonymous hemianopia, and ptosis of the left eye. The left pupil was dilated and reacting sluggishly. B.P. was 100/60 mm. Hg. Blood W.R. was negative. Other systems were normal. Angiography on the left side did not visualise the left internal carotid artery. She was treated with nicotinic acid 100 mg. thrice daily. She had recovered power on the right side but the ptosis showed signs of recovery only after about a year. There were no further episodes.

Case 4—B., male, aged 40, cultivator, was admitted on 19-2-1959 with inability to speak—duration two months. The onset was sudden during sleep. There was no loss of consciousness. Examination revealed slight weakness of the right side of the face, of the supranuclear type. The nervous system was normal in

other respects. Carotid pulsation was feeble on the left side. Other systems were normal. B.P. was 130/70 mm. Hg. Blood W.R. was negative. Angiography on the left side showed non-filling of the internal carotid artery ½ inch from the bifurcation (Fig. 2, *vide* Plate). He was put on nicotinic acid 100 mgm. t.d.s. and two weeks later the facial weakness had improved and the aphasia was persisting. The patient was seen about 8 months later. He had recovered speech with dysphasia persisting. There were no further attacks or episodes of weakness of any of the limbs.

Case 5—S.A.H., male, aged 55, pensioner, resident of Hyderabad was admitted on 2-11-1958 with left hemiplegia of 3 days' duration. The onset was sudden, the attack occurred as the patient was standing. He became drowsy and could be roused on deep stimulation. On examination the patient was found to be semiconscious. There was conjugate deviation of the head and eyes to the left side and left-sided hemiplegia including the face. Carotid pulsation was felt equally on both the sides. B.P. was 168/110 mm. Hg. Blood W.R. was negative. The neurosurgeon suspected a subdural haematoma and advised exploration with burr holes, which was done and no abnormality was noted. Later an angiography on the right side showed a complete blockage of the right internal carotid artery, a little away from the bifurcation (Fig. 3, *vide* Plate). The patient was treated on symptomatic lines. The coma gradually deepened and the patient developed pulmonary oedema and expired. No postmortem examination was done.

Case 6—L., male, aged 55, kirana merchant, resident of Brahminpalli Hyderabad, was admitted on 17-7-1959 with a right hemiplegia of 3 days' duration and aphasia of 1 day's duration. The onset was sudden and was preceded by giddiness. There was previous history of headaches and giddiness. Examination revealed that the aphasia was of the expressive type. There was gross diminution of vision in the right eye. Fundoscopy showed arteriosclerotic changes in both the fundi. Carotid pulsation was felt on both sides. B.P. was 190/120 mm. Hg. Blood W.R. was positive in 16 dilutions. Other systems were normal. Angiography did not visualise the left middle cerebral artery (Fig. 4, *vide* Plate). He was treated with serpasil 0·25 mg. twice daily for 5 days and priscol 50 mg. intramuscularly twice daily for 6 days. He had regained power in the limbs, with poor recovery of the finer movements. There was also difficulty in talking and the vision in the right eye had improved.

Case 7—H.B., female, aged 30, resident of Medak was admitted on 27-8-1958 with left crural monoplegia of one month's duration. The onset was sudden and was noticed when she woke up. There was no loss of consciousness and no prodromal symptoms. Examination revealed spastic monoplegia of the left lower limb with brisk jerks and extensor plantar. There were no bladder disturbances and no loss of cortical sensations. B.P. was 122/84 mm. Hg. Blood W.R. was negative. Carotid pulsations were normal. Angiography showed that the right anterior cerebral artery was not visualised (Fig. 5, *vide* Plate). She was treated with fersolate two tablets thrice daily for anaemia. She was also given a course of crystalline penicillin. She made a good recovery.

Case 8—T.N., male, aged 55, kirana merchant, was admitted on 12-9-1958 with quadriplegia of 3 days' duration. The complaint started with right hemiplegia 15 days before, for which he took some indigenous treatment which gave him some relief. Three days prior to admission he lost consciousness which lasted one hour. After regaining consciousness he observed loss of power in all the four limbs. Examination revealed quadriplegia, the right half of the body being more affected than the left, with brisk jerks and extensor plantar. The left plantar was equivocal. Carotid pulsations were normal. There were also dysarthria and slight dysphagia. B.P. was 130/80 mm. Hg. Blood W.R. was negative. A clinical diagnosis of basilar artery insufficiency was made. He was treated with nicotinic acid 50 mg. thrice daily and entodon 2 ml. intramuscularly for six injections. He recovered gradually and was able to walk and carry on with his normal duties. There were no further episodes.

Case 9—R.R., male, aged 60, was admitted on 7-11-1959 with headache, giddiness, dysphagia, dysarthria and ataxia of 3 days' duration. The onset was sudden, the complaints started with a severe intractable headache on the right side. It was followed by an intense vertigo and dysphagia. On examination, there was loss of all sensations, with loss of corneal reflex in the distribution of the 5th nerve on the right side. There was also palatal paralysis and cerebellar signs on the right side. B.P. was 136/80 mm. Hg. Blood W.R. was negative. Other systems were normal. A diagnosis of thrombosis of the right posterior inferior cerebellar artery was made. He was treated with a course of procaine penicillin, glucose 25 per cent 100 ml. intravenously daily and nasal feeding. Three weeks later he could swallow semisolid food and was able to stand and walk a few yards. There was no headache and vertigo. Slight dysarthria persisted.

Case 10—P., male, aged 50, merchant, resident of Shahabad was admitted on 17-11-1958 with loss of consciousness, dysphagia, and facial paralysis on the right side since the same evening. The onset was sudden, and started with vertigo and the patient became unconscious, remaining so for about 3 hours. Later he was semiconscious and noticed that he could not swallow. The next morning he regained consciousness completely. Examination showed nystagmus on looking to the right side. There was infranuclear type of facial paralysis on the right side. Motor power was normal with slight spasticity on the left side. All sensations were diminished on the left half of the body. The knee and ankle jerks on the left side were brisk with extensor plantar response. B.P. was 142/90 mm. Hg. Blood W.R. was positive. Other systems were normal. A clinical diagnosis of thrombosis of branches of the basilar artery supplying the lateral portion of the right pons was made. He was given nasal feeding, for the first few days, and a course of procaine penicillin. He was able to swallow on the 3rd day and made a good recovery.

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other respects. Carotid pulsation was feeble on the left side. Other systems were normal. B.P. was 130/70 mm. Hg. Blood W.R. was negative. Angiography on the left side showed non-filling of the internal carotid artery ½ inch from the bifurcation (Fig. 2, *vide* Plate). He was put on nicotinic acid 100 mgm. t.d.s. and two weeks later the facial weakness had improved and the aphasia was persisting. The patient was seen about 8 months later. He had recovered speech with dysphasia persisting. There were no further attacks or episodes of weakness of any of the limbs.

Case 5—S.A.H., male, aged 55, pensioner, resident of Hyderabad was admitted on 2-11-1958 with left hemiplegia of 3 days' duration. The onset was sudden, the attack occurred as the patient was standing. He became drowsy and could be roused on deep stimulation. On examination the patient was found to be semiconscious. There was conjugate deviation of the head and eyes to the left side and left-sided hemiplegia including the face. Carotid pulsation was felt equally on both the sides. B.P. was 168/110 mm. Hg. Blood W.R. was negative. The neurosurgeon suspected a subdural haematoma and advised exploration with burr holes, which was done and no abnormality was noted. Later an angiography on the right side showed a complete blockage of the right internal carotid artery, a little away from the bifurcation (Fig. 3, *vide* Plate). The patient was treated on symptomatic lines. The coma gradually deepened and the patient developed pulmonary oedema and expired. No postmortem examination was done.

Case 6—L., male, aged 55, kirana merchant, resident of Brahminpalli Hyderabad, was admitted on 17-7-1959 with a right hemiplegia of 3 days' duration and aphasia of 1 day's duration. The onset was sudden and was preceded by giddiness. There was previous history of headaches and giddiness. Examination revealed that the aphasia was of the expressive type. There was gross diminution of vision in the right eye. Fundoscopy showed arteriosclerotic changes in both the fundi. Carotid pulsation was felt on both sides. B.P. was 190/120 mm. Hg. Blood W.R. was positive in 16 dilutions. Other systems were normal. Angiography did not visualise the left middle cerebral artery (Fig. 4, *vide* Plate). He was treated with serpasil 0·25 mg. twice daily for 5 days and priscol 50 mg. intramuscularly twice daily for 6 days. He had regained power in the limbs, with poor recovery of the finer movements. There was also difficulty in talking and the vision in the right eye had improved.

Case 7—H.B., female, aged 30, resident of Medak was admitted on 27-8-1958 with left crural monoplegia of one month's duration. The onset was sudden and was noticed when she woke up. There was no loss of consciousness and no prodromal symptoms. Examination revealed spastic monoplegia of the left lower limb with brisk jerks and extensor plantar. There were no bladder disturbances and no loss of cortical sensations. B.P. was 122/84 mm. Hg. Blood W.R. was negative. Carotid pulsations were normal. Angiography showed that the right anterior cerebral artery was not visualised (Fig. 5, *vide* Plate). She was treated with fersolate two tablets thrice daily for anaemia. She was also given a course of crystalline penicillin. She made a good recovery.

Case 8—T.N., male, aged 55, kirana merchant, was admitted on 12-9-1958 with quadriplegia of 3 days' duration. The complaint started with right hemiplegia 15 days before, for which he took some indigenous treatment which gave him some relief. Three days prior to admission he lost consciousness which lasted one hour. After regaining consciousness he observed loss of power in all the four limbs. Examination revealed quadriplegia, the right half of the body being more affected than the left, with brisk jerks and extensor plantar. The left plantar was equivocal. Carotid pulsations were normal. There were also dysarthria and slight dysphagia. B.P. was 130/80 mm. Hg. Blood W.R. was negative. A clinical diagnosis of basilar artery insufficiency was made. He was treated with nicotinic acid 50 mg. thrice daily and entodon 2 ml. intramuscularly for six injections. He recovered gradually and was able to walk and carry on with his normal duties. There were no further episodes.

Case 9—R.R., male, aged 60, was admitted on 7-11-1959 with headache, giddiness, dysphagia, dysarthria and ataxia of 3 days' duration. The onset was sudden, the complaints started with a severe intractable headache on the right side. It was followed by an intense vertigo and dysphagia. On examination, there was loss of all sensations, with loss of corneal reflex in the distribution of the 5th nerve on the right side. There was also palatal paralysis and cerebellar signs on the right side. B.P. was 136/80 mm. Hg. Blood W.R. was negative. Other systems were normal. A diagnosis of thrombosis of the right posterior inferior cerebellar artery was made. He was treated with a course of procaine penicillin, glucose 25 per cent 100 ml. intravenously daily and nasal feeding. Three weeks later he could swallow semisolid food and was able to stand and walk a few yards. There was no headache and vertigo. Slight dysarthria persisted.

Case 10—P., male, aged 50, merchant, resident of Shahabad was admitted on 17-11-1958 with loss of consciousness, dysphagia, and facial paralysis on the right side since the same evening. The onset was sudden, and started with vertigo and the patient became unconscious, remaining so for about 3 hours. Later he was semiconscious and noticed that he could not swallow. The next morning he regained consciousness completely. Examination showed nystagmus on looking to the right side. There was infranuclear type of facial paralysis on the right side. Motor power was normal with slight spasticity on the left side. All sensations were diminished on the left half of the body. The knee and ankle jerks on the left side were brisk with extensor plantar response. B.P. was 142/90 mm. Hg. Blood W.R. was positive. Other systems were normal. A clinical diagnosis of thrombosis of branches of the basilar artery supplying the lateral portion of the right pons was made. He was given nasal feeding, for the first few days, and a course of procaine penicillin. He was able to swallow on the 3rd day and made a good recovery.

Case 11—K.H., male, aged 56, hakim, resident of Hyderabad was admitted on 17-12-1958 with inability to use the right upper limb of 15 days' duration. The onset was sudden and was preceded by subjective sensations of tingling and numbness. There was no loss of consciousness. Examination showed weakness of the right upper extremity with loss of all movements, and brisk jerks were present. Sensations were normal. B.P. was 160/100 mm. Hg. Fundoscopy showed grade-1 hypertensive retinopathy. Blood W.R. was strongly positive. Carotid pulsations were normal. He improved with antisyphilitic treatment. A clinical diagnosis of right brachial monoplegia due to thrombosis of a cortical branch of the left middle cerebral artery was made.

Case 12—Y.N., male, aged 55, retired police constable was admitted on 1-4-1959 with left hemiplegia and ptosis of the right eye of two months' duration. The onset was sudden with loss of consciousness. The patient gave history of exposure ten years back. On examination there was found a total paralysis of the right 3rd nerve with a lateral squint in the right eye and diplopia. The right pupil was dilated and did not react to light or accommodation. There was also diminished appreciation of all sensations on the left half of the body including the face. The deep reflexes on the left side were brisk, with extensor plantar response. B.P. was 170/120 mm. Hg. Blood W.R. was strongly positive. Other systems were normal. Carotid pulsations were normal. A clinical diagnosis of Weber's syndrome, as a result of thrombosis of a branch of the posterior cerebral artery supplying the right side of the midbrain was made. He was given a course of penicillin injections followed by a course of bismuth injections, after which he recovered power in the left half of the body, but the recovery from ptosis was poor.

Case 13—M.Y., male, aged 50, merchant, was admitted on 25-3-1959 with fever and severe headache of 8 days' duration. On examination, there was bilateral proptosis, with swelling and marked congestion of the conjunctivae. The movements of the eyes were restricted in all the directions and were painful. There was diplopia in the left eye. The pupils were equal on both sides. There was anaesthesia in the distribution of the first and second divisions of the left 5th nerve with loss of corneal reflex. Fundoscopy showed mild papilloedema with a few haemorrhages in both the eyes. There was no rigidity of the neck. There was no focus of infection in the area of drainage of the cavernous sinus. The patient was toxic with a temperature of 102°F. A clinical diagnosis of cavernous sinus thrombosis was made and was treated with crystalline penicillin 1 lakh units three-hourly and achromycin one capsule four times a day. The proptosis and congestion subsided and the temperature was normal. The anaesthesia of the first and the second divisions of the left 5th nerve and paralysis of the left 6th nerve were persisting.

Case 14—P., female, aged 25, resident of Hyderabad was admitted on 25-8-1959 with fever of 15 days' duration, and inability to walk, of 8 days' duration. The patient had a natural vaginal delivery at home two months ago. On examination she was found to be anaemic (Hb. 30 per cent, R.B.C. 1·49 million/c.mm.). The motor power was diminished on both sides, the right side being more affected than the left. The sensations were normal. The deep reflexes were brisk on both sides with extensor plantar on the right side and flexor on the left side. There was also incontinence of urine and faeces. The cortical sensations were intact. Fundoscopy showed bilateral papilloedema. A clinical diagnosis of superior sagittal sinus thrombosis was made and an angiogram was done, with a picture taken in the venous phase which did not visualise the superior sagittal sinus but visualised only the draining veins (Fig. 6, *vide* Plate). She was given blood transfusion on two occasions and dicrysticin for one week. She made a good recovery and was able to attend to her normal duties.

Case 15—H., female, aged 20, resident of Hyderabad was admitted on 30-9-1959 with unconsciousness since the previous day. She was delivered at home 17 days before. She was having high fever with rigors for the last 10 days with intense headache and gradual loss of consciousness.

Examination of the patient revealed toxaemia and anaemia. The patient was deeply comatose, without response to deep stimuli. Slight rigidity of the neck was present. Kernig's sign was negative. There was ptosis of the left eye, with inequality of the pupils, the left was dilated and not reacting. There was also loss of corneal reflex on the left side and right hemiplegia including face, with exaggerated deep jerks and extensor plantar response. There was proptosis of both eyes with congestion, and oedema of the conjunctivae. A clinical diagnosis of thrombophlebitis of the cavernous and superior sagittal sinuses was made. The patient was put on crystalline penicillin, 1 lakh units three-hourly, achromycin, one capsule four-hourly for one week and intrathecal penicillin 20,000 units daily for one week. The patient made a good recovery, except that ptosis of the left eye was persistent but was showing signs of recovery, at the time of discharge.

Aetiopathological Considerations

A clear understanding of the aetiopathology of cerebral thrombosis needs consideration of its anatomical and physiological aspects.

I. Anatomical Considerations :

Various irregularities of the cerebral vessels have been reported and these have an important place in the causation of the neurological deficit.

(a) In the cervical region, one or even both the carotids have been reported to be absent, the other carotid or the basilar making up for the deficiency.

(b) Variations in the size of the external-internal carotid anastomoses are a common finding.

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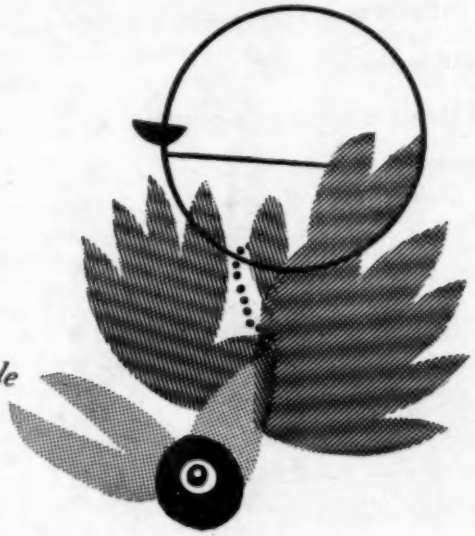

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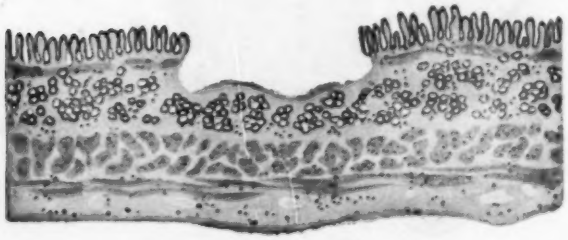

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(c) Inequality in the size of the vertebral arteries is almost the rule, the left usually being the larger. Their first intracranial branches, the posterior inferior cerebellars are often anomalous.

(d) Variations are numerous in the circle of Willis, a normal cofiguration being found in only 50 per cent of the cases.

(e) The circle of Willis is the most important source of collateral arterial supply to the brain through the anterior and posterior communicating arteries, permitting occlusion of one or even both the carotids, without consequent cerebral infarction. In addition to the circle of Willis, there also exist (i) anastomoses between the branches of the external and internal carotid arteries, and (ii) intrinsic anastomoses.

(f) The histological structure of the cerebral arteries is related to the method of regulation of the cerebral circulation. It has been observed by Wolff (1938) that the effect of the well-developed elastic internal lamina is to damp down the pulsation of the vessels, and it is obvious that in the closed box of the skull this could occur only at the expense of the surrounding brain tissue. Another striking feature is the tortuous intracranial course of the internal carotid artery known as the carotid syphon, and also a similar loop in the course of the vertebral artery between the atlas and the foramen magnum. The effect of these curvatures may well serve to damp down the transmitted arterial pulse.

II. PHYSIOLOGICAL CONSIDERATIONS :

The normal cerebral blood flow in young men at rest averages 54 to 65 ml. of blood per 100 g. of brain per minute, or approximately 750 ml. per minute through the entire brain ; the normal range is 500 to 1000 ml. (Kety, 1940 ; Himwich, 1951). The cerebral blood flow is dependent upon the cardiac output, blood pressure, peripheral resistance and the cerebrovascular resistance. The cerebrovascular resistance indicates the local impedance to the flow of blood through the brain, by friction of fluid against the internal walls of the vessels. It is calculated by dividing the mean arterial blood pressure by the estimated cerebral blood flow and equals the force (in mm. Hg) required to drive one ml. of blood through 100 g. of brain in one minute. The normal value is 1·6 mm. (Kety, 1940). An increased cerebrovascular resistance indicates diminution of cerebral blood flow, and is seen in arterial diseases such as arteriosclerosis, hypertension, and atherosclerosis. A decrease of cerebrovascular resistance indicates increase in cerebral blood flow and is seen in arteriovenous shunts as in cerebrovascular anomalies.

Another factor that is of considerable importance in the maintenance of cerebral blood flow is carbon dioxide which is the chief physiologically operative local regulator to obtain oxygen. Carbon dioxide is present as an end-product of cerebral metabolism and exerts an influence on the tone of the intracranial vessels.

III. AETIOLOGICAL FACTORS :

The principal aetiological factors are atherosclerosis, and syphilis. Other causes are polyarteritis nodosa, abnormal conditions of the blood like polycythaemia, septicaemic conditions, inflammatory conditions and pulseless disease.

The frequency of affection of the various cerebral arteries are as follows (Murphy, 1954) :

(a) Middle cerebral artery	...	75 per cent
(b) Posterior cerebral artery	...	10 per cent
(c) Basilar artery ...	...	10 per cent
(d) Anterior cerebral artery	...	5 per cent

The vulnerability of the middle cerebral circulation is due to the fact that the ganglionic vesesls are end-arteries, without any collateral source.

The factors responsible for precipitating thrombosis in an artery that has been affected by atherosclerosis are :

(a) When an habitually high B.P. is temporarily lowered and the circulation is less active, and

(b) Slowing of circulation in the area affected.

IV. PATHOLOGICAL CONSIDERATIONS :

The factors that influence the clinical manifestations as a result of thrombosis are :

(a) Anomalies in the circle of Willis may impair the adequacy of the collateral circulation.

(b) The vessels that take part in the collateral circulation may also be affected by the atherosclerotic process and do not carry sufficient blood to the area supplied by the thrombosed vessel. Hence the collateral circulation is of paramount importance in determining the clinical effect produced (Rob and Wheeler, 1957).

(c) The area of infarction of the brain from demonstrated occlusion of an artery is much less than its area of supply as shown by injection methods (Denny-Brown, 1951). For every cerebral vessel there must exist a zone of tissue critically dependent upon its integrity and a much wider area of network shared with the neighbouring

vessels for which the status of the tissue is for a time critical, but eventually stabilised following occlusion of the main vessel. Such a hypothesis may explain the mechanism of a transitory cerebrovascular episode which has been ascribed by some to vasospasm.

(d) The significance of recurrent cerebral ischaemic attacks is that it heralds the oncoming of a thrombosis. It is supposed to be caused by a severe atherosclerotic narrowing of the cerebral arteries. The patient manifests brief episodes occurring as attacks identical of focal disorders of brain function, depending on the areas affected ranging from hemiparesis or hemiplegia, quadriplegia, paraesthesia, dysarthria, dysphagia, etc., when the vertebrobasilar system is affected ; and with monocular blindness, contralateral hemiplegia and visual disturbances when the carotid system is affected. These attacks may be a few or several over a period of a few weeks or months and leaving no residual signs.

Discussion

There were 15 cases in the present series. Twelve were of arterial thrombosis and three of venous thrombosis. Eleven of them were males and four were females. The ages of the patients ranged from 20 to 60 years. There was no family history of paralysis or strokes except in two cases (Cases 6 and 10) who gave the history of their parents having died of hypertension.

Cases 1 to 5 :

These were the cases of carotid artery thrombosis proved by angiography and confirmed by repeating the angiography about a week later. Case 2 was that of common carotid thrombosis and Cases 1, 3, 4 and 5 were those of internal carotid thrombosis.

Laterality of the lesion—Of the 5 cases, 4 were on the left side and 1 was on the right side. Ameli and Ashby (1949) in a review of 33 cases of carotid thrombosis observed that 24 were on the left side and 9 were on the right side. In Andrell's (1943) series of 23 cases, 16 were on the left side and 7 were on the right side. In their series of 8 cases, Ramamurthy and Balaparameswara Rao (1959) found that 6 were on the right side and 2 were on the left side. They observed that there was no special significance to the laterality of the lesion. The reasons for this peculiar predominance on the left side are not known but it has been suggested by Hendrick and Andrew (1954) that it may probably be due to the difference in the anatomy on the two sides.

Sex incidence—Of the 5 cases, 4 were males and 1 female. In their review Ameli and Ashby (1949) have found 5 out of 33 reported cases to be females. In their series of 8 cases reported by Ramamurthy and Balaparameswara Rao (1959), 5 were males and 3 females. It would thus be seen that the disease is predominant among the males.

Age incidence—Of the 5 cases presented here, one was in the second decade, two in the third, one in the fourth, and one in the fifth decade. In their series of 33 cases, Ameli and Ashby (1949) found that 14 were in the sixth decade and 11 in the fifth, the rest being distributed in the other decades. Of 8 cases reported by Ramamurthy and Balarameswara Rao (1959), the youngest patient was aged 11 years and the oldest 55 years. The ages of the other patients were distributed as follows: 1 in the second decade, 3 in the third, and 2 in the fourth decade. Teng and Goldenberg (1960) described a case of thrombosis of the left internal carotid artery at the syphon in a child aged 5 years, manifesting repeated convulsions.

Role of syphilis—In none of the present series, was there a history of venereal disease, nor was the blood positive for syphilis. Moniz (1947) was of the opinion that in the aetiology of carotid thrombosis, syphilis stood out as the most important cause and was followed by other causes, but it is difficult to agree in view of the fact that in his series of 6 cases, only one gave a history of syphilis (but blood W.R. was negative). It is the opinion of Sorgo (1939) that atherosclerosis was the cause of carotid artery thrombosis.

Role of hypertension—Out of the 5 cases in this series, only Case 5 had mild hypertension (168/110 mm. Hg). The rest of the cases had their blood pressures within normal limits.

Palpation of the carotid artery—Carotid pulsation was felt in Cases 1, 3 and 5, and was found diminished in Case 4 and was absent in Case 2. Great stress had been laid on the palpation of the carotid artery (Hunt, 1914). In Case 2, in which the common carotid was occluded at the bifurcation, no pulsation was felt. In the other cases it was doubtful whether the pulsation that was felt was from the external carotid vessel or the internal carotid vessel. Palpation of the internal carotid by pharyngeal method as advocated by Dunning (1953) was not done in the present series. In a patient with signs and symptoms suggestive of internal carotid thrombosis, palpation of the carotid for pulsation does not exclude occlusion of the artery. This can be confirmed only by angiography.

Episodes of carotid insufficiency—In the present series only Case 3 had symptoms suggestive of an insufficiency occurring earlier.

Symptomatology — The symptomatology of internal carotid artery thrombosis is varied. The artery may get gradually occluded without the appearance of any symptoms, provided there is sufficient collateral circulation. In the present series, Case 5 had left-sided hemiplegia of sudden onset with loss of consciousness. Case 1 had papilloedema on the left side together with right-sided hemiplegia. Case 2 had aphasia with right hemiplegia. Case 3 had ocular palsies in the left eye, right homonymous hemianopia and right-sided hemiplegia. Case 4 manifested as aphasia of the expressive type with supranuclear type of facial weakness on the right side. In the series of 8 cases reported by Ramamurthy and Balaparameswara Rao (1959), 3 presented with papilloedema, 2 had ocular palsies, 3 had mental symptoms and 2 did not have any weakness of the contralateral limbs.

It would thus be observed that cases of carotid thrombosis present themselves with symptoms ranging from headache, convulsions, mental changes, ocular palsies and focal signs with or without papilloedema which may suggest and be mistaken for a space-occupying lesion. It is therefore important to keep the condition in mind and confirm or exclude by angiography.

The role of ophthalmodynamometry in the diagnosis of insufficiency or thrombosis of the internal carotid artery has been advocated by Hollenhorst (1958). He observed that the pressure on the occluded side is from 25 to 50 per cent of the pressure recorded on the normal side. However if the pressures are equal on both the sides, occlusion is not ruled out.

Recovery—All the patients in the present series were treated on symptomatic lines. One patient (Case 5) had died and the death must have been due to an extensive infarction and poor collateral vascular supply. The other cases who have been followed for a period of about a year made good clinical improvement. Treatment of the condition by re-establishment of the carotid circulation has been suggested recently, by anastomosing the external carotid to the distal end of the internal carotid after excision of the thrombosis portion. This is possible only if the thrombosed segment is small in length with a patent vessel above. Restoration of the circulation is ideal and is worth attempting in all cases where possible, otherwise the burden of the cerebral circulation is carried alone by the opposite carotid and any lesion of the sole-surviving carotid may result in a catastrophe.

CASES 6-15 :

Case 6—This was a case of occlusion of the main trunk of the middle cerebral artery on the left side, which gave rise to a picture of extensive motor, sensory and speech disturbances. He had hypertension and his blood W.R. was strongly positive.

Case 7—This was a case of left crural monoplegia of sudden onset, due to occlusion of the right anterior cerebral artery. Occlusion of this artery usually causes crural monoplegia with or without cortical type of anaesthesia and at times bladder disturbances. In this case there were no disturbances either of sensations or of the bladder.

Case 8—This case was one of basilar artery insufficiency. The diagnosis was based on (i) the clinical finding of hemiplegia on the right side 15 days before and later followed by weakness of all the limbs and dysarthria and (ii) the recovery of the patient.

Case 9—This patient had a characteristic clinical picture of thrombosis of the posterior inferior cerebellar artery on the right side. Prognosis of this condition is good and the patient made a complete recovery.

Case 10—This patient was admitted with a clinical picture diagnostic of lateral pontine syndrome. His blood W.R. was positive. The cause of thrombosis was probably syphilis.

Case 11—This case was a middle-aged man who was admitted with right brachial monoplegia of sudden onset. There were no other neurological signs. The cortical sensations were normal. He had hypertension and his blood W.R. was positive. He improved with antisyphilitic treatment.

Case 12—The clinical picture of this case was diagnostic of Weber's syndrome. His blood W.R. was positive. He improved with antisyphilitic treatment.

Case 13—This was a case of cavernous sinus thrombosis. Cavernous sinus thrombosis though unilateral to start with usually involves the other side also by extension across the anastomotic vessels. He made a good recovery.

Case 14—This patient had the clinical picture of superior sagittal sinus thrombosis, which was confirmed by angiography. The aetiology was due to puerperal sepsis. She responded very well to antibiotics and supportive treatment.

Case 15—This was a case of simultaneous involvement of the cavernous and the superior sagittal sinuses from an infective focus in the pelvic veins as a result of puerperal sepsis. She made a remarkable recovery with antibiotics and supportive treatment.

Summary

15 cases of cerebral thrombosis are presented. The varied manifestations of carotid artery thrombosis are discussed. The incidence of cerebral thrombosis and other relevant features are dealt with.

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OBSERVATIONS ON ACQUIRED APLASTIC ANAEMIA*

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Aplastic anaemia without any apparent cause continues to be a serious haematologic disorder. While the myelotoxic propensity of a variety of exogenous factors is well known, in practice in many cases of aplastic anaemia, it is not possible to link up the haemopoietic depression with any known myelotoxic agent or drug (Mohler and Leavell, 1958; Scott *et al.*, 1959; Chatterjea, 1960). Such cases in the present state of our ignorance are usually labelled as idiopathic. It appears that instances of such idiopathic cases are being encountered more often during recent years.

These cases show varying grades of peripheral pancytopenia, usually with grossly depleted bone marrow and clinical symptoms depending mainly on the degree of haemopoietic depression. Ultimate prognosis depends on the nature and degree of myelodepression. In instances of mild and reversible damage, bone marrow may recover if properly nurtured during the depressed phase. When the marrow is severely damaged, prognosis is usually unfavourable, though not invariably fatal as in leukaemia. In the absence of exact knowledge regarding the aetiology and lack of "real" myelostimulatory agents, treatment remains mainly supportive supplemented with measures mostly empirical.

In view of the lack of adequate knowledge on this "ever-recurrent haematological problem", a comprehensive investigation was undertaken to characterise the disorder as met with in India and to elucidate its aetiopathogenetic aspects. The present communication is an account of 31 cases of the disorder.

Material and Methods

The series of 31 patients were investigated and followed up in Calcutta mostly during the period 1956-1959. The total number of patients with haematological disorders examined during this

* Adapted from a paper presented at the VIII International Congress of Haematology, Tokyo, Japan, September, 1960.

period was 3,200. Ages of the patients varied from 7 to 57 years. There were 25 males and 6 females. In the adult group, the occupational status was: student 8, petty businessman 5, clerk 1, mechanic 2 and administrative job 3. All the females were housewives. Of the 7 children, 5 were students. 25 patients were from Bengal, 3 from Bihar, 2 from Rajasthan, 1 from Uttar Pradesh and 1 from Bombay. There were 25 Hindus, 5 Muslims and 1 Parsi.

In addition to routine clinical and haematological examination (including repeated bone marrow examination), the investigtions were done from the following aspects:

A. Immunologic tests to detect the presence of antibodies active against red cells, white cells and platelets (Coombs *et al.*, 1945; Dacie, 1954; Stefanini *et al.*, 1953; Moeschlin and Schmid, 1954).

B. Erythrocytic fragility tests to measure the osmotic and mechanical fragility of red cells before and after incubation (Dacie, *loc. cit.*; Shen *et al.*, 1944), plasma haemoglobin (Bing and Baker, 1931).

C. Levels of alkali resistant haemoglobin (Singer *et al.*, 1951) and haemoglobin electrophoretogram (Chatterjea *et al.*, 1956).

D. Studies with Cr^{51} to measure the survival of patient's red cells in his own circulation and with Fe^{59} to measure the bone marrow function (Annual report, Haematological Unit, I.C.M.R., 1959-1960).

E. Tests to evaluate the possible role of any deficiency with reference to vitamin B_{12}, folic acid, protein, iron and thyroid activity (Annual report, Haematological Unit, I.C.M.R., 1958-59).

F. Response to steroid hormones and splenectomy.

Observations

CLINICAL:

The onset was insidious in 21 cases while in the remaining 10 it was fairly rapid in evolution. The usual presenting features were weakness refractory anaemia, unexplained fever and haemorrhages from skin and mucous membrane. Slight enlargement of spleen was noted in 3 patients.

History of exposure to myelotoxic drug was obtainable only in one patient, a 22 year old Parsi girl, who had been receiving dilantin sodium for the last 5 years.

BLOOD:

Haemoglobin varied from 1·7 to 7·5 g./100 ml., R.B.C. from 0·5to 2·3 mill./c.mm., P.C.V. from 6 to 25 per cent. and reticulocytes from 2,200 to 52,650 per c.mm. In 8 cases, P.C.V. was below 10 per cent. Total W.B.C. varied from 1,050 to 4,200/c.mm., neutrophils from 122 to 2,688 and lymphocytes from 442 to 3,034/c.mm. Total W.B.C. count was below 3,000/c.mm. in 19 cases, neutrophil count below 1,000/c.mm. in 15 cases and lymphocyte count below 1,000/c.mm. in 11 cases. Platelet count varied from 730 to 80,000/c.mm.

BONE MARROW:

Repeated examinations were done in all cases. In 25 cases, marrow was grossly hypocellular involving all elements. In this hypocellular group, lymphocytes and plasma cells constituted the main cellular element. In one case, there was a very significant increase of lymphocytes suggesting an absolute increase of these cells. In another case there was similar increase of plasma cells. In 19 cases, tissue mast cells were significantly increased.

In 6 cases, the marrow was in general cellular. Megakaryocytes were, however, decreased in all cases. Erythropoiesis was significantly depressed in 5. Significant depression of granulopoiesis was seen in 3. Tissue mast cells were increased in 5 and plasma cells in 6 cases.

Haemosiderin content was in general increased.

OTHER INVESTIGATIONS:

A. *Immunologic tests—*

(1) Coombs' test (direct) was positive in 5 cases.

(2) Tests for the detection of antibodies in serum.

Detectable titre of cold agglutinins was seen in 8 cases. In 4 cases, the agglutinins were detectable in both saline (1:2 to 1:16) and albumin (1:2 to 1:64) media. Indirect Coombs' test was positive in 2 cases.

(3) Tests for antileucocyte antibody—Employing the technique of Moeschlin and Schmid (*loc. cit.*), with homologous human leucocytes of the same ABO blood group as antigen, clear cut agglutination was observed in 11 cases.

(4) Tests for antiplatelet antibody—Employing the technique of Stefanini *et al.* (*loc. cit.*), human platelets of the same ABO group as that of the patient were used as the antigen. Clear cut agglutination was seen in 6 cases.

B. *Tests to measure the stability of red cells*—

(1) Osmotic fragility was tested in graded hypotonic saline solutions. Haemolysis started at a mean value of 0·393 per cent (range 0·32–0·48 per cent) saline and was complete at a mean value of 0·26 per cent (range 0·08–0·30 per cent) saline solutions.

(2) Mechanical fragility—Mean value was 2·5 per cent and the range varied from 0–9 per cent. In 2 patients the value exceeded 5 per cent (Normal value: mean 1·8 per cent, range 0–4·8 per cent).

(3) Incubation fragility—Samples of sterile defibrinated blood were incubated at 37°C under oil for 24 and 48 hours respectively. Osmotic fragility of the incubated samples was estimated. Mean value for the onset of haemolysis after 24 and 48 hours' incubation was 0·59 per cent (range 0·36–0·76 per cent) and 0·7 per cent (range 0·6–0·96 per cent) saline respectively. Haemolysis was complete at a mean value of 0·227 per cent (range 0·12–0·32 per cent) and 0·27 per cent (range 0·08–0·8 per cent) saline respectively.

(4) Plasma bilirubin—The mean value was 0·45 mg. with a range varying from 0·2–0·8 mg. per 100 ml.

(5) Plasma haemoglobin—With the modified technique of Bing and Baker (*loc. cit.*), the basic plasma haemoglobin level varied from 0–26 mg. per cent (mean 4·6 per cent). In 9 cases, the value exceeded 5 mg. per cent. The mean plasma Hb. levels in the plasma obtained from whole blood incubated at 37°C for 24 and 48 hours were 124 mg. (range 3·2–500) and 341 mg. (range 15·5–8,400) per cent respectively.

C. *Alkali resistant haemoglobin and haemoglobin electrophoretogram*—

(1) Alkali resistant haemoglobin — With Singer's technique, the mean value was 6·4 per cent and the range varied from 0·46–17·5 per cent. In 10 cases, the value exceeded 5 per cent.

(2) Haemoglobin electrophoretogram — Two subjects were found to have the pattern of Hb.E in heterozygous state.

D. *Studies with Cr^{51} and Fe^{59}**—

The gross half life of Cr^{51}-tagged red cells in two cases was 20·5 and 21·5 days respectively (normal half life 25–34 days).

The rate of plasma clearance was slow being 160 and 124 minutes in 2 cases of aplastic anaemia. The uptake by red cells was, however, poor being respectively 16 and 28 per cent. (In normal subjects the values for plasma clearance were 72–89 minutes, while those for uptake of Fe^{59} by red cells were 74–82 per cent).

The half life of donor's cells was estimated in 3 cases. In one with tagged red cells the half life was 23 days. In two others with Ashby technique the half life was 26 and 60 days respectively.

E. *Tests to evaluate the role of deficiency factors*—

(1) Serum vitamin B_{12} was estimated microbiologically with *Euglena gracilis var bacillaris*. Mean values for free and total serum vitamin B_{12} were 209 $\mu\mu$g. (range 0–760) and 567 $\mu\mu$g. (range 40–1,760) per ml. In 10 cases, free vitamin B_{12} level exceeded 200 $\mu\mu$g. In 2 cases, values for total vitamin B_{12} were below normal, being 80 and 40 $\mu\mu$g./ml. respectively ; both these patients were vegetarians ; parenteral vitamin B_{12}, however, did not improve blood picture in either case.

Analysis of the ratio of free to total vitamin B_{12} showed that in this disorder the free fraction was relatively more increased comprising on an average about 31 per cent of total fraction (mean normal value 10–20 per cent). The details of these findings were discussed elsewere (Banerjee *et al.*, 1960).

(2) Vitamin B_{12} binding capacity of serum—Incubated under standard condition with 5,000 $\mu\mu$g. of vitamin B_{12}, the mean value was 494 and the range varied from 250–775 $\mu\mu$g./ml. (normal values ; mean 1248, range 600–2,425 $\mu\mu$g./ml.). Thus the binding capacity was depressed.

(3) Serum folic acid was estimated microbiologically with *Streptococcus faecalis R* as the test organism. The mean serum folic acid level was 2·02 mμg./ml. and the range varied from 0·5–6·75 mμg./ml. (normal value: mean 4·37, range 1·5–15mμg./ml.).

(4) Folic acid excretion in urine before and after a test dose of folic acid given subcutaneously —Mean basic excretion of folic acid was 7·74 μg. and the range varied from 0·134–36 μg. in 24 hours. Mean excretion after injection of a 5 mg. test dose was 1·07 mg. and range varied from 0·26–2·49 mg. in 24 hours (normal values: basic excretion–mean 0·0032 μg./ml., range 0·001–0·009 μg./ml. ; after a test dose–mean 2·58 mg., range 1·45–3·72 mg. in 24 hours.

(5) Serum iron and iron binding capacity—Mean serum iron level was 207 μg. (range 65–360 μg.) per cent. The unsaturated iron binding capacity was reduced ; mean 98 μg. (range 0–200 μg.) per cent. Iron saturation was high.

* In collaboration with Dr. F. Hosain and Dr. B. D. Nag of Saha Institute of Nuclear Physics, Calcutta.

(6) Serum proteins—Total serum protein varied from 4·8 to 7·9 g. per cent with a mean value 5·9 g. The differential pattern of protein spectrum is shown in Table 1.

TABLE 1—SHOWING DIFFERENTIAL PATTERN OF PROTEIN SPECTRUM

	Mean (per cent)	Range (per cent)
Albumin	38·6	26·2—56·4
Globulins		
Alpha$_1$	5·4	3·8—10·7
Alpha$_2$	10·6	5·1—17·17
Beta	16·6	8·0—26·9
Gamma	28·9	12·7—38·4

(7) Blood cholesterol—Total blood cholesterol varied from 160 to 350 mg. per cent with a mean value of 180 mg. per cent. The value, 350 mg., was obtained in only one, a patient with diabetes mellitus ; in the remaining, the highest value was 223 mg. per cent.

(8) Basal metabolic rate (BMR)—The rate ranged from +1 per cent to −12 per cent.

F. *Therapeutic response*—

Most of the patients had already received the various haematinics including vitamin B_{12}, folic acid, vitamin C and iron, but without any effect.

Patients were treated in main with repeated blood transfusions, steroid hormones (ACTH, cortisone, prednisone and perandren) and other supportive measures, as necessary for the control of infection and alleviation of associated complications. In the present series, available data did not suggest any significantly specific benefit attributable either to perandren or to prednisone group of drugs.

Of the 31 cases, 16 died ; 4 died within 1 month, 2 within 2 months, 9 between 3 to 6 months and 1 within 1 year. Four cases could not be followed up for final assessment.

The remaining 11 cases showed varying degrees of improvement. In one case, blood picture became completely normal within 9 months ; in another, followed up for 32 months, R.B.C. and W.B.C. showed normal values though platelet level continued to be low. Four patients are maintaining themselves with periodic transfusions. The other five cases were splenectomised. In three, improvement has been very significant ; followed up so far for 20, 32 and 10 months respectively they are still maintaining more or less normal blood values. In the fourth patient there was slight clinical imrpovement with no significant haematological improvement ; this patient was lost sight of 14 months after splenectomy and could not be followed further. The fifth patient has shown slight clinical and haematological improvement.

COMMENTS

Twenty-five cases of the present series conformed to the classical picture of aplastic anaemia as described originally by Ehrlich. In the remaining 6, the marrow preparations were in general cellular ; the haematopoiesis was, however, grossly inadequate with direct or indirect evidence of hypoplasia involving megakaryocytes and one or the other element. Study and follow-up of similar cases described in literature under such varied terms as aplastic or hypoplastic anaemia, aregenerative or adynamic anaemia, have tended to indicate that bone marrow function and bone marrow morphology correlate but poorly in so far as the maintenance of circulating cellular elements of blood is concerned. Whatever confusion there may be in the realm of nomenclature, there is at present a more or less uniform agreement regarding the identity of the condition under discussion. Broadly speaking, the condition may be defined as one characterised by peripheral pancytopenia due to gross anatomical and functional inadequacy of bone marrow. No primary disease—infection, metabolic dyscrasia, endocrine disorder, neoplasia, or any other known affection—can be incriminated as having any definite casual relationship. It appears that the two broad groups—classical aplasia (25 cases) and the group with cellular marrow (6 cases)—may have an aetiologic unity.

The sequence of changes in bone marrow when exposed to myelotoxic agents may vary depending on the nature of the agent and the period of exposure. The individual susceptibility would constitute a third variable in determining the nature and degree of bone marrow damage. It is thus possible that the cellular, the hypoplastic and the aplastic bone marrow patterns as seen in the present series of patients are illustrative of the different phases of the same disorder. The general clinical and haematological features in these subjects would fit in with this broad concept of bone marrow aplasia.

Results of vitamin B_{12} and folic acid assays in blood and urine did not show any evidence of deficiency. Serum protein values did not present any significantly abnormal pattern.

Serum iron level, iron binding capacity of serum and bone marrow haemosiderin presented a pattern which may be explained on the basis of a large amount of available iron that cannot be utilised due to inadequate erythropoiesis.

The relative increase of free vitamin B_{12} fraction is an interesting finding which has not been previously reported. It may be related to the depressed binding capacity of serum for vitamin B_{12}. The increase of free vitamin B_{12} and depressed binding capacity of serum are, to some extent, comparable to what is seen with reference to iron and may in all probablity be secondary to inadequate erythropoiesis (Banerjee *et al.*, *loc. cit.*).

All these data would show that in an average case of aplastic anaemia there is no deficiency, direct or indirect, of protein, iron, vitamin B_{12} and folic acid. Judged by blood cholesterol level and BMR, hypothyroidism was unlikely to be of any aetiologic significance.

There was no evidence pointing to any intrinsic defect of circulating red cells. Slightly abnormal fragility test, the results of Coombs' test and Cr^{51} studies would indicate that some of the circulating red cells in a proportion of these patients are destroyed in an abnormal way. Presence of leucoagglutinins and thromboagglutinins would indicate that some of these circulating cells are perhaps destroyed in an abnormal way and presumably at an abnormal rate. Isoimmunisation process stimulated through multiple transfusions was no doubt partly responsible for the presence of these anomalous agglutinins.

In refractory cases, the results of splenectomy were found to be encouraging. It appears that when other therapies had failed, the question of splenectomy should be seriously considered. In such a desperate situation even partial benefit is worth striving for.

Summary

Results of investigative and follow-up study in a series of 31 cases of aplastic anaemia in Indians are briefly reported. In an average case, there was no evidence of any known deficiency factor or any significant intra-erythrocytic defect. Interesting findings were (i) presence of leucoagglutinins and thromboagglutinins, (ii) increase of free fraction of serum vitamin B_{12} and (iii) elevated level of alkali resistant haemoglobin.

In refractory cases, the results of splenectomy were encouraging.

ADDENDUM :

Follow-up report on the *Splenectomised subjects* show that in November 1961, the three patients are still maintaining normal blood values, now after 36, 48, and 26 months following splenectomy. The fourth patient was lost sight of as already indicated. The fifth patient still maintains his slightly improved status, 20 months after splenectomy.

Acknowledgment

Grateful thanks are due to Dr. R. N. Chaudhuri, Director, School of Tropical Medicine, Calcutta, for giving necessary facilities for this study and to Dr. B. D. Nag and Dr. F. Hosain of the Saha Institute of Nuclear Physics for collaboration in the radioactive studies. Sincere appreciation is due to Dr. R. N. Ray and Dr. Sandhya Ghose for their help in the study. Indebtedness is expressed to Professor J. C. Banerjea for the opportunity to study one patient under his care and to Prof. Kumar Kanti Ghosh and Dr. Subrata Banerjea for their admirable collaboration in the surgical management of the five patients.

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Fig. 1—Left carotid angiogram showing that the left internal carotid system was not filled, but only the external carotid and its branches were filled (Case 1)

Fig. 2 — Left carotid angiogram showing non-visualisation of the internal carotid artery, but visualisation of the external carotid and its branches (Case 4)

Fig. 3—Right carotid angiogram showing non-visualisation of the right internal carotid artery (Case 5)

Fig. 4 — Left carotid angiogram showing filling of the anterior cerebral artery and its branches. The left middle cerebral artery is not visualised (Case 6)

Fig. 5 — Right carotid angiogram showing filling of the right middle cerebral artery. The right anterior cerebral artery is not visualised (Case 7)

Fig. 6—Right carotid angiogram (the picture was taken in the venous phase) showing non-visualisation of the superior sagittal sinus but only visualises the draining veins (Case 14)

RAO—*Cerebral Thrombosis (p. 529)*

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Fig. 7—Skiagram of the chest. Right oblique view with barium in the oesophagus showing displacement due to enlarged left auricle (Case 3)

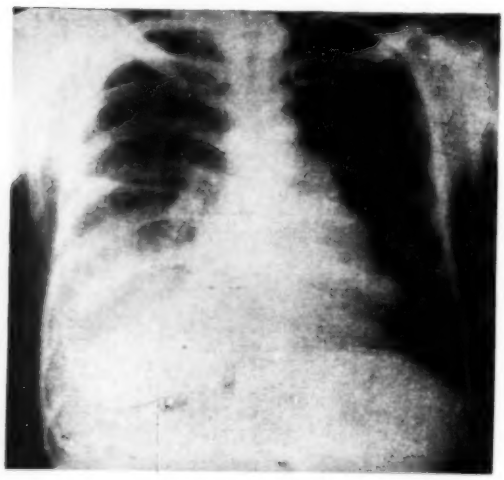

Fig. 8—Skiagram of the chest. Postero-anterior view showing mitralisation, thickening of the right interlobar fissure and hazy opacity at the right base (Case 3)

SEPAHA *et al*—*Mitral Stenosis without Diastolic Murmur (p. 543)*

Fig. 1 — Dissected heart showing : 1—Trunk of left coronary artery. 2—Anterior interventricular branch of left coronary artery. 3—"Deep sternocostal branch" supplying the deeper aspect of right sternocostal surface. 4-5—Right and left flaps respectively of the anterior interventricular groove after absorption of interventricular septum. 6—Intercoronary anastomosis

CHATTERJEE—*A Study of Coronary Vascular System(p. 547)*

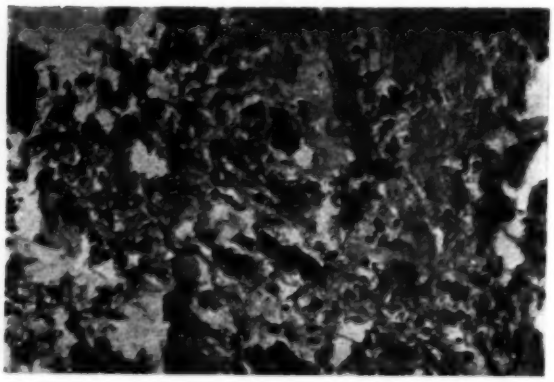

Fig. 2—Photomicrograph showing destruction of muscle tissue by malignant cytotrophoblastic type of cells (Case 1)

HAZRA AND PAUL—*Chorionepithelioma (p. 557)*

MITRAL STENOSIS WITHOUT DIASTOLIC MURMUR

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AND

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In mitral stenosis, an accurate diagnosis is very essential because of the possibility of surgical relief. In an average case, a routine examination is enough and the diagnosis is easy because of the characteristic physical signs like slapping apex beat, diastolic thrill, opening snap and rough diastolic murmur supported by the fluoroscopic and electrocardiographic findings. Even the presence of a rough diastolic murmur alone is enough for the diagnosis of mitral stenosis. An elaborate haemodynamic study is not essential in an average case but occasionally there are cases where the murmur may be inaudible and the diagnosis a bit difficult.

Three cases of mitral stenosis with inaudible diastolic murmur, who came under our observation in the M. Y. Hospital, Indore, during the last four years, are being reported. Two of them were confirmed on postmortem examination. The auscultation of all the cases was done independently by at least five persons at different times and also after exercise and no diastolic murmur could be heard in any of the cases.

Case Reports

Case 1—B.S., aged 28 years, was admitted on 6th October, 1956, with complaints of dyspnoea on exertion and cough with slight expectoration of 2 years' duration, with a history of haemoptysis 10 months back. Palpitation, more so on exertion, and dull constant pain in the right hypochondrium were present for the last one year.

He had pain in knee and elbow joints, 1½ years back, which lasted for about 15 days but was not associated with swelling of the joints or fever. He used to take a moderate quantity of alcohol and smoked about 10-15 'beedis' a day till one year back.

Physical examination—He was of an average build, had cyanotic tinge, neck veins were full and oedema was present over the feet. Apex beat was palpable in the 5th intercostal space, ½" outside the mid-clavicular line. There was parasternal lift and epigastric pulsation of the right ventricular type and the heart was enlarged on both sides. Mitral first sound was loud and slightly rough and pulmonary second sound was accentuated. There was a soft systolic murmur close to the left border of the sternum which diminished markedly on deep inspiration and did not show any selective propagation towards the axilla. Lungs showed crepitations all over and liver which was palpable 1½" below the costal margin was soft, tender and did not show any systolic pulsation. Spleen was not palpable.

Investigations—Total R.B.C., 4·8 million per c.mm.; Hb., 14 g. per cent; total W.B.C., 8,050 per c.mm. with neutrophils 65 per cent and lymphocytes 35 per cent. Erythrocyte sedimentation rate, 20 mm. first hour (Wintrobe's corrected) and blood Kahn's test, negative. Urine showed no abnormality.

Fluoroscopy showed straightening of the left border, pulmonary conus +, Roots +, R.V. +, L.A. + and no definite systolic expansion.

E.C.G. (Fig. 1) revealed right ventricular hypertrophy.

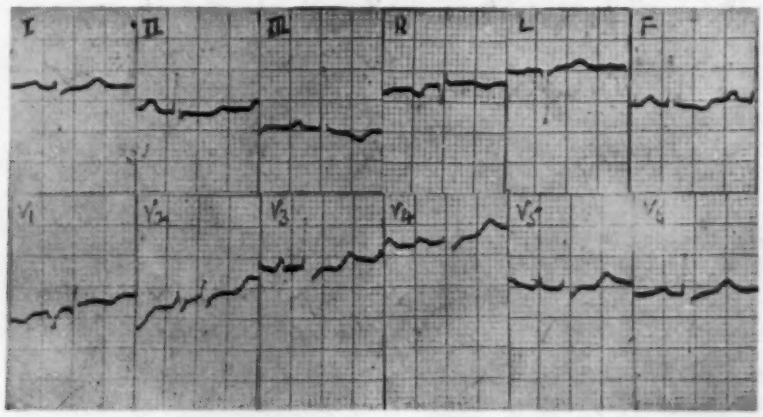

Fig. 1—Electrocardiogram (Case 1) Showing Right Ventricular Hypertrophy Pattern

Diagnosis—Chronic rheumatic endocarditis and mitral stenosis with congestive cardiac failure.

Treatment—He was treated for cardiac failure and on 24th January, 1957, developed cough, haemoptysis and pain in the chest and expired.

Postmortem findings—The mitral valve showed a gross degree of stenosis with calcification and could admit only the tip of the little finger (Fig. 2). The

FIG. 2—SPECIMEN OF HEART (CASE 1) SHOWING HYPERTROPHY OF THE LEFT AURICLE AND STENOSIS OF THE MITRAL VALVE. R.A.=RIGHT AURICLE. L.A.=LEFT AURICLE.

left auricle and right ventricle were hypertrophied and dilated. Tricuspid and aortic valves were normal. The lungs were congested and the left lung showed infarction in the lower lobe. The other viscera showed evidence of chronic venous congestion.

Comments—The case was under our observation for nearly 3½ months and suddenly died of pulmonary infarction. Though no diastolic murmur was heard at any time, there were other evidences, clinical as well as fluoroscopic and electrocardiographic, which enabled us to label him as mitral stenosis which was finally confirmed on postmortem examination.

CASE 2—T., aged 30 years, was admitted with history of gradually progressive exertional dyspnoea and cough with occasional expectoration of 6 years' duration. There were pain in the right hypochondrium, more on pressure, and oedema over the feet for the last 4 months. He had haemoptysis 8 months back and an attack of rheumatic arthritis at the age of 13 years.

Physical examination—He looked cyanosed and slightly breathless but still could lie in bed without much discomfort. The neck veins were full, showed prominent systolic pulsation and oedema was present over the feet and abdominal wall. Pulse was 90 per minute, B.P. 100/90 mm. of mercury, respiration 28 per minute and temperature 98·6°F. Apex beat was poorly palpable in 5th intercostal space about ½" outside the mid-clavicular line. There was slight parasternal heave, pulmonary second sound palpable and the heart was slightly enlarged on both sides. On auscultation, the mitral first sound was loud and pulmonary second sound was accentuated and split. There was a systolic murmur, best heard at the lower border of the sternum, which increased in intensity on deep inspiration and sitting position and did not show selective propagation towards the axilla. Lungs showed evidence of emphysema and scattered râles and rhonchi on both sides, more towards the bases. Liver was 3" enlarged below the costal margin, soft, tender and showed systolic expansile pulsation.

Investigations—Total R.B.C., 4·6 million per c.mm.; Hb., 13·5 per cent; total W.B.C., 9,800 per c.mm. with 67 per cent neutrophils, 27 per cent lymphocytes, 2 per

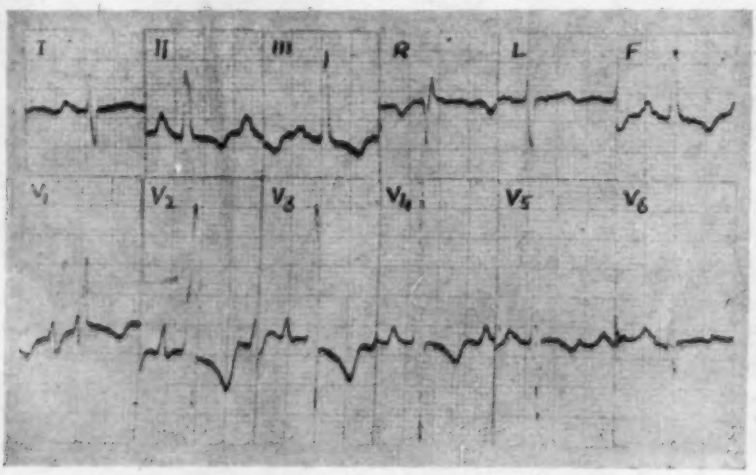

FIG. 3—ELECTROCARDIOGRAM (CASE 2) SHOWING RIGHT BUNDLE BRANCH BLOCK WITH HYPERTROPHY (R' IN V_1=11 MM.)

cent large monocytes and 4 per cent eosinophils. Blood E.S.R. was 24 mm. 1st hour (Wintrobe's) and blood Kahn's test was negative. Urine showed a trace of albumin but no casts.

Fluoroscopy showed straightening of the left border, R.V. +, R.A. +, L.A. + and no definite systolic expansion. Diaphragmatic pulsation +; Lungs congested.

E.C.G. (Fig. 3) revealed right bundle branch block with hypertrophy (R' in V_1=11 mm.).

Diagnosis—Chronic rheumatic endocarditis with mitral stenosis, tricuspid incompetence and congestive failure.

Treatment—He was put on treatment for congestive failure but gradually became worse and expired on 19th February, 1959.

Postmortem findings—The mitral and tricuspid valves showed evidence of healed rheumatic processes. The mitral valve showed a gross degree of stenosis just allowing the tip of the little finger only and also showed calcification. The tricuspid valve showed incompetence and could admit easily 4 fingers (Fig. 4). The right ventricle, right auricle and left auricle were hypertrophied and dilated (Figs. 4 and 5). The aorta and pulmonary arteries right up to the terminal branches showed evidence of atherosclerosis. The other organs showed chronic venous congestion. The kidneys showed congenital anomaly in the form of horse-shoe kidney with absence of pelvis in both the organs. The ureter on either side was formed by separate ureterules originating from each calyx.

Comments—The patient was admitted with cardiac failure and there was clinical evidence of tricuspid incompetence. Though there was no definite diastolic murmur in the mitral area; presence of loud mitral first sound, accentuated and split pulmonary second sound, slight parasternal heave (not well marked possibly because of emphysema) and electrocardiographic evidence

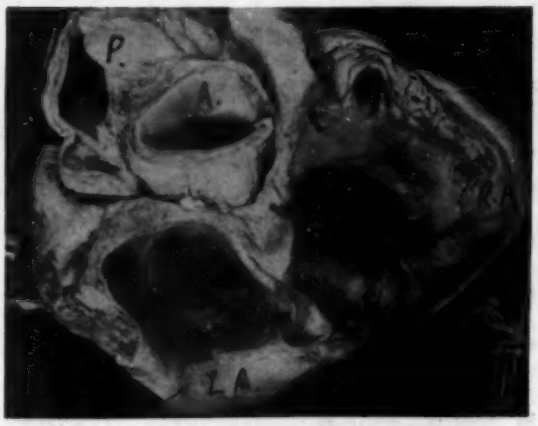

FIG. 4—SPECIMEN OF HEART (CASE 2) WITH AURICLES OPENED SHOWING HYPERTROPHY OF LEFT AND RIGHT AURICLES. THE MITRAL VALVE IS STENOSED WHILE THE TRICUSPID VALVE SHOWS INCOMPETENCE. L.A.=LEFT AURICLE. R.A.=RIGHT AURICLE. A.=AORTA. P=PULMONARY ARTERY

FIG. 5—SPECIMEN OF HEART (CASE 2) WITH VENTRICLES OPENED SHOWING HYPERTROPHY AND ENLARGEMENT OF THE RIGHT VENTRICLE. R.V.=RIGHT VENTRICLE. L.V.=LEFT VENTRICLE.

of right bundle branch block with hypertrophy and fluoroscopic evidence of enlargement of right ventricle and left auricle were enough to suspect very strongly mitral stenosis which was finally confirmed on postmortem examination.

CASE 3—M., aged 35 years, was admitted on 22-12-1959, with complaints of gradually increasing exertional dyspnoea of 2 months' duration, pain and lumpy feeling in the right hypochondrium and oedema over the feet for the last 15 days. There was no history of rheumatism in the past and none of the family members suffered from hypertension.

Physical examination—An adult male lay in bed with back rest, having a puffy face with cyanotic tinge, orthopnoeic, neck veins full and oedema present all over the body, more marked on the feet. Pulse was 88 per minute, regular; blood pressure 150/100 mm. of mercury, temperature 99°F and respirations were 34 per minute. Apex beat was diffusely felt in the 5th space, ½" outside the mid-clavicular line. No thrill was palpable anywhere and on percussion the heart was enlarged on both sides. Auscultation revealed loud mitral first sound and accentuated second sound at the base, the pulmonary one being more accentuated than the aortic. There was a soft musical systolic murmur, best heard just inside the apex beat; it showed marked respiratory variation and no selective propagation towards the axilla. Chest was emphysematous and râles and rhonchi were heard all over both sides, more towards the bases. There was slight oedema of the abdominal wall and shifting dullness could be elicited. Liver was 3" enlarged below the costal margin, soft, tender

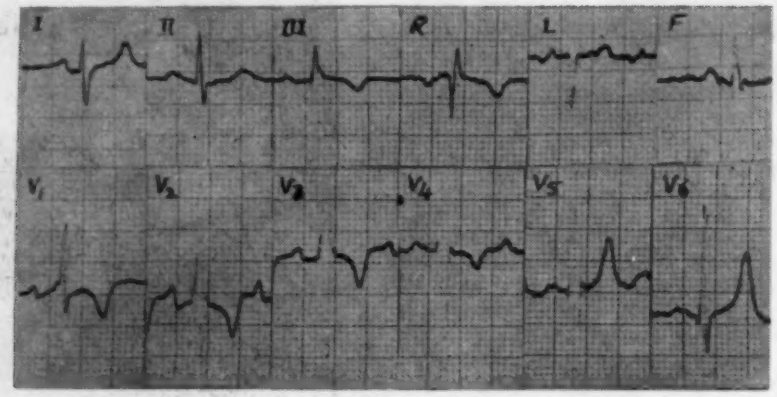

FIG. 6—ELECTROCARDIOGRAM (CASE 3) SHOWING RIGHT VENTRICULAR HYPERTROPHY PATTERN

and did not show any expansile pulsation. Spleen was just palpable.

Investigations—Urine on 17-12-1959 showed a distinct trace of albumin, no sugar and microsocpic examination did not reveal any abnormality. On 28-12-59 even albumin was absent. Total R.B.C. was 4 million per c.mm., haemoglobin 14 g. per cent and total leucocytes 5,150 per c.mm. with neutrophils 60 per cent and lymphocytes 40 per cent. Blood urea was 32 mg. per cent, E.S.R. 12 mm. 1st hour (Wintrobe's) and blood Kahn's test negative.

Comments—On clinical examination alone a diagnosis of hypertension and both-sided failure was made and treatment started. After 2-3 days a routine electrocardiogram was taken (Fig. 6) which showed right ventricular hypertrophy pattern and fluoroscopic examination revealed congested pulmonary fields, prominent right interlobar fissure and enlargement of both the ventricles and also of the left auricle of the heart (Fig. 7, *vide* Plate). The E.C.G and fluoroscopic findings could not be explained and hence the case was re-examined with a view to find out if there was any associated valvular disease. No diastolic murmur was detected but with loud mitral first sound, accentuated pulmonary second sound, E.C.G. and fluoroscopic evidence, there was sufficient ground to label the case as one of mitral stenosis with a mild degree of essential hypertension. The musical systolic murmur appeared to be of functional nature because of marked change in intensity on deep inspiration, no selective propagation and its disappearance after about a week with the improvement of cardiac failure. Cardiac catheterisation was performed on 15-1-60 and the results are given in Table 1.

TABLE 1—SHOWING RESULTS OF CARDIAC CATHETERISATION (CASE 3)

Prsesure		Right auricle	Right ventricle	Pulmonary artery
Systolic	...	15	37·5	37·5
Diastolic	...	7	0	20
Mean	...	8	18	26

He was discharged from the hospital on 27-1-1960 and called for a check up in July 1960. At this time he gave a history of pain in the chest, cough and haemoptysis about a month back. Skiagram of the chest revealed a patch of opacity in the right base, possibly pulmonary infarct (Fig. 8, *vide* Plate) and the cardiac findings were the same. The evidence of pulmonary infarct further confirmed the suspicion of mitral disease.

DISCUSSION

Three cases of mitral stenosis have been presented who did not show any diastolic murmur on examination. One of the well known causes, where the murmur may be inaudible, is onset of ectopic rhythm with rapid rate, especially auricular fibrillation to which these cases are very prone. With fibrillation the presystolic murmur disappears and the early diastolic rumble may only be heard during relatively long pauses. Paroxysmal tachycardia, either supraventricular or ventricular, may also make the murmur inaudible. None of our cases had ectopic rhythm at any time. With sinus rhythm the absence of a diastolic murmur is rather uncommon, though well known.

Wood (1956) stated that the murmur may be masked by gross enlargement of the right ventricle secondary to an extreme pulmonary resistance, for the left ventricle may then be displaced so far posteriorly that mitral events may not be audible at the apex. Secondly, if there is an extreme degree of pulmonary hypertension, the murmur may be practically inaudible as the blood volume coming to the left auricle is relatively small. The other causes can be an extreme degree of mitral stenosis causing a markedly enlarged left auricle and tricuspid incompetence. In the former, the trickle of blood through the valve is poor because of tight stenosis while in the latter less blood goes to the

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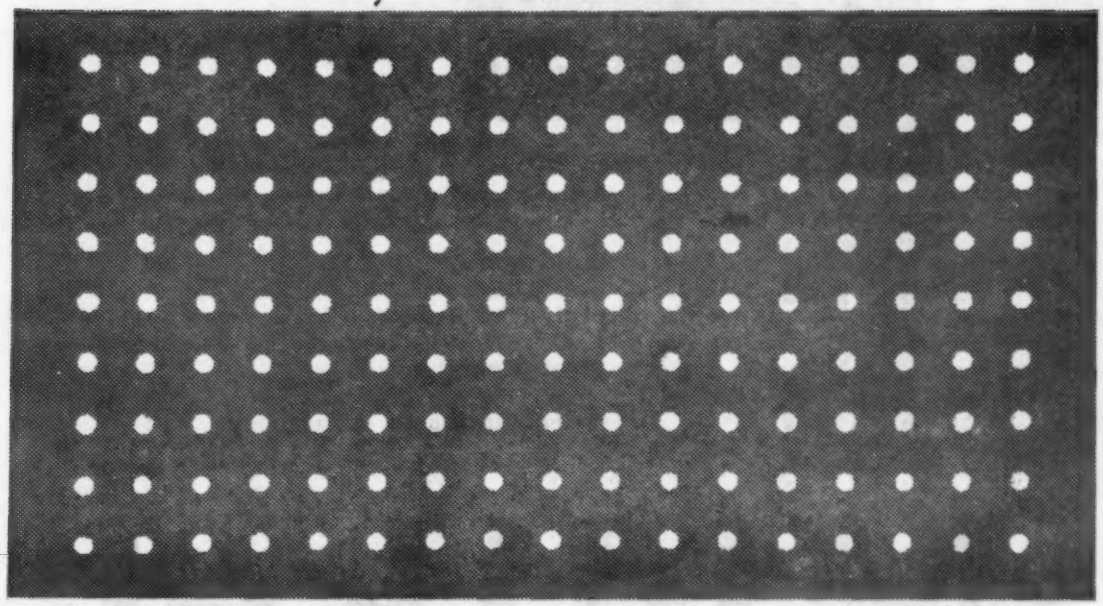

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pulmonary circulation resulting in reduced left auricular filling. In cases where the murmur is inaudible usually more than one factor operates.

In Case 2 all the above factors were operating. He had tight mitral stenosis with clinical evidence of pulmonary hypertension and tricuspid incompetence. In Case 1 also all the factors were operating except tricuspid imcompetence. In Case 3 there was a moderate degree of pulmonary hypertension as shown by catheterisation study, some degree of systemic hypertension and both-sided failure. The extra factor present in this case was systemic hypertension and left ventricular failure. In the presence of left ventricular failure the diastolic pressure in the left ventricle will be raised and then the flow of blood through the mitral valve may be so much reduced as not to produce a well marked murmur. This factor associated with the other factors could be responsible for the inaudibility of the diastolic murmur in the third case.

Summary and Conclusions

1. Three cases of mitral stenosis without any diastolic murmur are presented along with post-mortem reports of 2 cases

2. The factors responsible for inaudibility of the diastolic murmur were thought to be marked pulmonary hypertension, rotation of the heart, extreme degree of mitral stenosis and tricuspid incompetence.

3. Left ventricular failure as one of the possible causes of damping down the murmur is discussed.

Acknowledgment

Our grateful acknowledgments are due to Dr. S. K. Mukerji, Emeritus Professor of Medicine, for his valuable criticism and to Dr. C. M. Rangam, Professor of Pathology for his autopsy findings. Our thanks are also due to Dr. B. C. Bose, Principal, M. G. M .Medical College, Indore, and Dr. R. Bhattacharya, Superintent, M. Y. Hospital, Indore, for permission to publish the case reports.

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A STUDY ON CORONARY VASCULAR SYSTEM

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In a previous communication on this subject (Chatterjee, 1960) we pointed out a very important fact that the sternocostal surface of the right ventricle close to the infundibulum on its superficial aspect is the least vascular area. It was also mentioned that a small artery like the infundibular branch of the right coronary could not possibly supply such a big area. It was presumed that this area must have been receiving its blood supply from other sources, probably from the intercoronary anastomosis running through the interventricular septum connecting the anterior interventricular branch of the left coronary artery with the inferior interventricular branch of right coronary artery.

Materials and Methods

With a view to find out the probable sources of blood supply to this area, further investigations were carried out. We started our work with neoprene latex and obtained fresh human hearts from accident cases. A total of 32 normal human hearts of different ages varying from 23 to 40 years was studied. There was no history of abnormality or hypertension in any of these cases. The method adopted was the same as described in our previous paper (Chatterjee, *loc. cit.*).

Observations

The sternocostal surface of the right ventricle on its superficial aspect close to the infundibulum shows the same type of distribution and the existence of the same 'least vascular area' as mentioned before. But in the series of last 7 hearts by separating the right and left ventricles along the interventricular groove, which is opened by absorption of interventricular septum (Fig. 1, *vide* Plate), the following important observations were made which provide a clear explanation for the existence of the 'least vascular area' on the superficial surface.

1. There is a rich intercoronary anastomosis running through the interventricular septum connecting the anterior interventricular branch of the left coronary artery with the inferior interventri-

cular branch of the right coronary artery. From this anastomosis numerous minute branches are given off to the deeper aspect (ventricular aspect) of the sternocostal surface of the right ventricle.

2. Secondly, another big branch, derived from the left coronary artery where it gives off an anterior interventricular branch, or from the anterior interventricular branch itself, is given off which passing through the anterior interventricular groove, enters the right ventricle and then crosses it obliquely to reach the deeper aspect of the sternocostal surface of the right ventricle. We propose to call this branch 'deep sternocostal branch' of the left coronary artery. This is, in our opinion, a pretty big branch which is responsible for blood supply to the 'least vascular area' from its ventricular aspect.

3. It is well-known that the conducting system of heart or neuromyocardium consists of (a) the sinoatrial node, (b) the atrioventricular node and (c) the A.V. bundle of His and its branches together with the subendocardial plexus of Purkinje's fibres. Through this system the rhythmic impulses of heart propagate. The A.V. bundle extends from the A.V. node situated in the interatrial septum beside the opening of coronary sinus to the ventricular septum passing through the fibrous part of the skeleton of heart. It skirts the hinder part of membranous interventricular septum behind the medial cusp. At the junction of membranous and muscular part of the interventricular septum, the A.V. bundle divides into right and left branches. The right branch passes over the right surface of the interventricular septum of the right ventricle under the endocardium and is then distributed to anterior papillary muscles along the moderator band. The left branch similarly passes over the left surface of the septum and ends at the base of the papillary muscles of the left ventricle dividing into anterior and posterior branches. From the facts stated above this big arterial branch has a great clinical significance.

4. The area of the right ventricle, i.e., the upper part of the sternocostal surface including the anterior septal regions appears to have the least vascularity but actually it is supplied by the intercoronary anastomosis as well as by the deep sternocostal branch as demonstrated earlier. This artery arising from the left coronary artery and traversing through the interventricular septum subendocardially, comes in contact with the right branch of the A.V. bundle. Thus the right banch of A.V. bundle also gets a supply from this arterial twig.

A possible clinical implication of this anatomical observation may be the occurrence of auriculoventricular block or bundle branch block as a result of an infarct produced in the anteroseptal region involving chiefly the upper part of the interventricular septum. The area of the right ventricle which is shown as less vascular, but is actually supplied from its deeper aspect by the deep sternocostal branch and intercoronary anastomosis, is less likely to be affected in the process of infarction ; and signs, including electrocardiographic signs, may not be obvious when the heart block is suddenly produced. A progressive occlusion of the deep sternocostal branch may also be responsible for an insidious onset of heart block as a feature of ischaemic heart disease.

Summary

1. Least vascularity in a fairly wide area on the superficial aspect of the right ventricle close to the infundibulum is a constant finding.

2. Numerous minute branches from intercoronary anastomosis enter the deeper aspect of that surface to supply that area.

3. A big branch arising from the left coronary artery where it gives off the anterior interventricular branch or from the anterior interventricular branch itself and passing through the anterior interventricular groove, goes deep into the sternocostal surface of the right ventricle. The author calls it 'deep sternocostal branch' of the left coronary artery which is responsible mainly for the blood supply of that area. That area is, therefore, supplied both by the 'infundibular branch' of the right coronary and the 'deep sternocostal branch' of the left coronary artery.

The A.V. bundle is supplied also by the 'deep sternocostal branch' of the left coronary artery and by intercoronary anastomosis.

Acknowledgment

Our grateful thanks are due to Dr. A. B. Mukherjee for encouragement and clinical interpretation of the subject matter of this paper, to Principal K. N. Bagchi for his valuable help in solving many difficulties in the course of this investigation and to Dr. A. K. Dutta, Demonstrator of Anatomy, C.N.M.I. for his invaluable assistance.

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SPECIAL ARTICLE

NEW ORAL HYPOGLYCAEMIC AGENTS IN NON-HORMONAL THERAPY OF DIABETES MELLITUS

Experience in Seventy Cases*

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Since the discovery of insulin in the treatment of diabetes in 1921, various efforts had been made to find out its oral substitutes. Synthalin, a diguanidine derivative, was found to be a good hypoglycaemic agent in physiological experiments, but its clinical trial resulted in a disaster because of its fatal toxicity (Frank *et al.*, 1926 ; Hesse and Traubmann, 1929). So instead of further experiments on oral therapy attention was paid to the improvements in duration of action of insulin, diet regimens, management of ketosis and other complications, and to proper organisation of diabetic clinics. The following 20 years of insulin therapy in diabetes mellitus achieved an increased life expectancy in diabetics. But neither a smooth control of diabetes, nor a comfortable diet or a life free from complications was obtained. In spite of increasing doses of insulin, many diabetics frequently suffered from severe muscular aches, boils, carbuncles, ketosis and many other complications. This was perhaps due to improper institution of insulin therapy, before normalisation of body weight and before judging the stabilisation on smaller amounts of insulin (Hoffman, 1960). No notice was taken of the fate of endogenous insulin production influenced by non-physiological hormonal therapy (Sterne, 1960) with large amounts of insulin for the immediate suppression of hyperglycaemia. In such complications, the blame was generally placed on dietary indiscretions or mental or physical over-exertion by the patient. Various types of diet regimens most of which included carbohydrate restrictions, sometimes with total exclusion of certain types of food or widely diversified exchange schedules, were recommended.

Duncan (1958) made the first rational approach to the importance of insulin therapy in diabetes. He held that "requirements of up to 100 units of insulin could be omitted by diet and weight reduction". In ketosis, however, he recommended immediate administration of 100 units of insulin for every plus of plasma or urinary acetone (Lee and Duncan, 1956). He saw the necessity of relieving the mild diabetics from insulin injection by simple diet regimen for achieving weight reduction.

Insulin overdosage was reported by many workers (Landabure *et al.*, 1959). This is very often seen in improperly supervised diabetics. Very quick fixation of insulin dosage from the percentage of sugar present in the urine, instead of watching the metabolic stabilisation by weekly average of 24 hours' urine sugar excretions (or of fasting blood sugar levels) at certain dose of insulin. For, the large dose of insulin required to suppress hyperglycaemia or glycosuria may be much larger than the real insulin requirement for the metabolic stabilisation of the diabetic state. Even pancreactomised patients do not need more than 20-30 or 50 units of insulin daily (Davidson, 1953). The authors have stabilised growth-onset (juvenile) diabetics on much lesser dose than what is taken by many maturity onset type of diabetics. Clinicians often forget the blocking effect of exogenous insulin on endogenous insulin production (when the action of the previous one is over), and the part played by antagonistic factors like glucagon, pituitary, adrenals and other hormones in the inactivation of large doses of insulin. This fact can be verified by the higher level of glycosuria in the fasting urine than in the postprandial stage in most cases of the overdosed diabetics. In such cases, it would not be possible to prevent fasting glycosuria by increasing the dose of long-acting insulin, unless that leads the patient to hypoglycaemia at odd hours. Complications do not always appear to be due to lesser dose of insulin, but they may be due to improper overdosing. Exogenous insulin administration can compete with endogenous insulin in amounts but not in metabolic regulation. Hence, an improper administration of insulin may aggravate a diabetic condition, which can otherwise be satisfactorily controlled by weight reduction and by diet control.

The notions of strict carbohydrate restrictions and avoidance of sugar and starch are now being abandoned. Burger (1959) allows up to 5 g. of carbohydrate per kg. body weight, and Haist (1960) has proved the necessity of carbohydrate in the food if endogenous insulin production is to be maintained and islet growth is to be continued. One should not, therefore, worry about mild post-

* In collaboration with C. S. Agarwal, N. D. Kanchan, M. G. Mohimtura, H. N. Maniar, W. F. Manquis, S. G. Oza, I. C. Patel, M. B. Popat, K. B. Rathi and P. R. Vakil, general practitioners in Bombay.

prandial glycosuria due to carbohydrate in diet when fasting blood glucose is within the controlled range.

It was a mere accident that the hypoglycaemic action of sulphonamides was discovered in 1942 by Janbon at Montepellier in France. Loubatieres (1946) established the clinicial usefulness of sulphanilylthiadiazoles (RP-2254) and glybuthiazoles (RP-2259). In spite of successful experiments, commercial exploitation of similar compounds like BZ-55 (carbutamide) and D-860 (tolbutamide) was delayed till 1955. Their pancreatropic action, through direct stimulation of islet cells, to produce and release endogenous insulin was demonstrated as early as 1944 by Loubatieres (1946). With sulphonylureas as a tool for investigation, a drastic change in our belief of islet cell function has been evidenced, and successful therapy with these drugs has opened up new concepts which consider that diabetes mellitus is not only caused by a deficit of islet cells but also by the sluggishness or inefficiency of the insulin secretory mechanism due to lack of proper stimulation of existing islet cells (Haist, 1960).

The first arylsulphonamide or sulphonylurea (carbutamide) was not so potent but had a good half life of 40 hours. Due to its higher dosage and tendency to accumulation, its amino group produced toxic reactions. This drawback was remedied by removing its amino radicle and substituting methyl radicle in the para position of aryl group of this compound (McLamore *et al.*, 1959). This led to the preparation of tolbutamide. Though the toxicity was very markedly decreased, the duration of action (and potency) of tolbutamide was drastically reduced to 4 hours, due to metabolic oxidation of its methyl group to the inactive p-carboxy derivative in liver (Stowers *et al.*, 1958). This resulted in the jittering action of immediate extreme hypoglycaemia at one hour and gradual loss of hypoglycaemic effect within six hours. Clinically, it produced severe appetite and consequent weight gain in diabetics. (At present, tolbutamide is also used for weight gaining therapy in normal persons). The high incidence of cardiovascular and cerebrovascular accidents with tolbutamide is suspected to be due either to this sudden and severe hypoglycaemic action, or due to the onset of secondary failure. Secondary failures which are found to be so common with tolbutamide might be due to the increased capacity of the organism (body) to do its carboxylation. In spite of repeated doses of tolbutamide, the diabetics who really need constant stimulation to islet cells cannot be controlled smoothly. We now need a sulphonylurea with a high potency for minimising toxic reactions at therapeutic dosage range. It should also possess a very long duration of action to induce constant islet cell stimulation and ensure smooth 24 hours' control of hyperglycaemia. Further experiments on thousands of similar compounds have revealed that maximal potency and duration of action are seen when chlorine or bromine was substituted in the para position (McLamore *et al.*, 1959), like the substitution of halogens in adrenocortical hormones for augmenting some of their physiological actions (Gordon, 1959). Chlorpropamide was found to be ideal in the group of such compounds possessing high potency and long duration of activity. Metahexamide was another very highly potent compound with the half life of about 8 hours ; but after extensive trial it was abandoned because of its latent toxicity. Furfurylurea is also reported to be a potent, long acting and effective drug even in slightly elevated blood glucose levels ; but it is not exploited commercially because it is three times more toxic than tolbutamide.

Prompted by some success of sulphonylureas, investigation was undertaken with other compounds which did not have any pancreatropic activity but had action on peripheral utilisation of glucose. Synthalin was re-examined, and its analogue biguanides were put into clinical trial. Biguanides, which are found to be absolutely free from toxicity (Krall and Bradley, 1959) seem to act by carrying out anaerobic glycolysis of glucose to the stage of pyruvates and lactates (Wick *et al.*, 1958). Though the mode of action is peculiar for every biguanide compound, all of them are found to facilitate entry of insulin into cells and to exert a generalised insulin sparing action (Sterne, 1960). Strangely enough, they have no hypoglycaemic action in normal persons and they produce the symptoms of nausea, metallic taste in mouth, diarrhoea and other gastro-intestinal derangements. Among biguanide compounds, phenethylbiguanide or 'phenformin' or DBI and N'N' dimethylbiguanide or 'glucophage' or LA-6023 are widely utilised. The former preparation is very potent and was largely investigated in U.S.A., while the latter one is mild and popular in Europe. DBI causes starvation type of ketosis, while glucophage is found to be free from this effect due to a different type of metabolism in the body (Sterne, 1960).

There is another interesting compound, p-oxypropiophenon, which does not have any hypoglycaemic effect by itself, but it produces a peculiar antidiabetic action through inhibition of the pituitary. Hence, it has been found to be extremely useful in the treatment of insulin

resistant diabetes. Other non-specific hypoglycaemic agents include salicylates which augment the action of chlorpropamide in suitable cases.

Laboratory Investigations

The following investigations were undertaken for diagnosis and control:

I. URINE AND BLOOD SUGAR TESTS:

Presence of postprandial urine sugar, or fasting blood glucose level above 100 mg. (Nelson, 1944) or a level above 140 mg. one hour after a carbohydrate meal, or its failure to return to 100 mg. level at two hours (or postprandial level above 120 mg.) confirmed the diagnosis of diabetes mellitus.

Importance was given to the initial oral glucose tolerance test, as the fasting blood glucose level is not a satisfactory index of severity. It was performed to estimate the diabetic status and to assess the renal threshold. Sometimes it was delayed till the fasting urine sugar became negative. The glucose meal of 100 g. which is utilised for the detection of diabetes was found to be unsuitable. When the glucose load of 1 g. per kg. body weight was utilised in the patients weighing over 150 lb., the curves obtained by us showed delayed peak and decline (mostly an ascending plateau). So, a minimum of 50 g. and a maximum of 70 g. in males, and 60 g. in females according to 1 g. glucose per kg. body weight are utilised for the proper estimation of the peak time and the delay in decline. Insulin was stopped at least 24 hours before and chlorpropamide was not administered on the morning of glucose tolerance test. Because, a severe diabetic uncontrolled with 100 units of insulin, was seen to shift the delayed peak time of 90 minutes to 45 minutes when glucose tolerance test was done within 12 hours of insulin administration.

Follow-up glucose tolerance tests were also done to determine the peak time by taking two suitable blood samples after a test meal, together with more frequent urine sugar determinations. Sometimes, the patient was also instructed to perform the test by estimating total and per sample urine sugar passed after a test glucose meal. Postprandial blood glucose test was purposely avoided as it is primarily designed for the detection of diabetes and because variability of Indian cooking and process of digestion makes it difficult to evaluate the test. Even though, the estimation of total urine sugar at three hours after a particular meal is found to be very reliable index to evaluate the control.

Much importance cannot be stressed upon fasting, peak or 2-hour glucose level in glucose tolerance test; but the time when the level starts to decline (or peak time) is found to be very important for judging the response to sulphonylurea therapy. We found that all the diabetics who show peak within an hour respond to chlorpropamide within a week, unless exceptions including technical errors in the test are present. These cases are mainly composed of: (a) untreated but mild and compensated diabetics, and (b) all the diabetics well treated with insulin. Some of the insulin treated severe diabetics respond to chlorpropamide, but lack of smooth control may be feared later on (e.g. with B29, B31, C6, C9). All the untreated or poorly treated diabetics with decompensated metabolism show typical curve having peak after 90 minutes or an ascending plateau and they are liable to respond to chlorpropamide after some delay period of up to 6 weeks (Beaser, 1960).

II. TESTS TO DETERMINE THE SEVERITY OF DIABETES:

In a severe diabetic, fasting blood glucose level is above the renal threshold of 140 mg. and after glucose meal administration, it goes on rising till two hours or more according to the absorption rate due to the lack of insulin action. It does not return to the fasting level even at three hours, and sometimes it goes on rising because of an upset in the hormonal balance caused by large amounts of glucose in the blood. In such cases, we cannot distinguish between the amounts of blood glucose derived from the food and those from the breakdown of tissue protein. This gluconeogenesis can be estimated roughly by increased total lipids (from a normal of 0·6 to 2·0 per cent or above) and by cholesteral levels of higher than 250 mg. They indicate the transport of fat to liver for the formation of ketones. Hence, the presence of ketones in plasma and urine indicates acutely decompensated energy metabolism and the patient may not respond to chlorpropamide alone.

III. OTHER TESTS:

We had utilised liver function tests, kidney function tests and haemograms whenever they were necessary.

Diet

Statistical data collected by British workers show a very remarkable decrease in the diabetic mortality during the period of war rationing and

slumps. This fact indicates that the quantity of food is the offending factor, rather than the carbohydrate. Landabure *et al.* (1959) quote their experience gained at the Institute of Nutrition of Argentina: "Regardless of the group in which a diabetic is classified, a basic factor of treatment is a balanced diet that normalises body weight." The requirement of insulin is roughly proportionate to the body weight in pounds. As recent research emphasises the importance of carbohydrate load for efficient beta cell function, we did not restrict carbohydrates much but paid more attention to well regulated low calroic diet and weight reduction. We advise dietary regimen according to the body weight of the patient and the condition of the diabetic.

I. REDUCING DIET FOR OVERWEIGHT PATIENTS:

Eating is a habit and dieting or the weight reduction is also a psychological problem. The approach must, therefore, be more psychological and practical rather than purely medical. When an overweight maturity onset diabetic does not have any acute complication, he may be advised only to cut down his daily meals to half of his usual. Prescribing of low carbohydrate or low caloric diet is very theoretical to be adopted by a person who has gained in weight by overeating of a spoonful a day for a number of years. He must reduce his weight within a number of days in order to obtain quick and maximum therapeutic benefit from the dieting and the drug. Many of these diabetics, however, care more for the quantity of food rather than the type, and they are always afraid of losing strength by eating less. It takes some time before the stomach is educated to a habit of eating moderately. Derivatives of amphetamine suppress appetite. A new anorexiant, phenmetrazine (preludin), induces a very powerful appetite-curbing effect and a sense of well being in overweight diabetics.

Different types of diet schedules are useful, and low calorie diet should be the aim, rather than the low carbohydrate diet. Proteins also contain almost the same amount of carbohydrate molecules as the starchy foods (plus nitrogen). So liberal amounts of proteins or carbohydrates mean the same in terms of dieting. Prescribed restricted foods create a kind of psychological apprehension in the patient's mind which makes the weight reduction a problem. Moreover, the value of foodstuff does not remain the same, and in Indian cooking, the size of *chapati* may vary from one to eight times in weight and *dal* can be anything from a clear soup to a thick gravy in different homes.

One should restrict butter, ghee and fried things, and should consider butter and oil four times and fried things twice as restricted as sugar in quantity. Rice and potatoes should be allowed in a quantity with which postprandial urine sugar does not go beyond 1 per cent. Pulpy vegetables are slightly more liberally allowed than rice; while leafy vegetables are encouraged as they fill up the stomach easily. Fresh fruits having large water content can be allowed, but a glassful of fruit juices should be prohibited. Pulpy fruits, like banana and mango, should be considered in the class of pulpy vegetables. Meat can be considered more harmful than rice, because of its high calorie value due to its fat content and less water content after cooking. Occasionally small amounts of sweets are allowed, but the patient should be advised to compensate them by cutting down the other items of the meal. To avoid hunger pain, one can encourage an allowance of a strong cup of tea or a glass of buttermilk or lemon squash (only with saccharine) just before meal, and fruits or coffee after the meal.

One should always be particular to ask the patient to keep a record of daily meals, dose of medicine, and the findings of urine examination. The dose of oral hypoglycaemic agents should be adjusted to keep the fasting urine sugar free and fasting blood glucose around 100 mg. The dose of the drug required to suppress postprandial glycosuria should not cause hypoglycaemic symptoms, as passage of up to 2 per cent of urine sugar after meals seems to be harmless (1 per cent sugar in daily 2000 ml. of urine amounts to 20 g. or only four heaped teaspoonfuls of sugar). Passage of postprandial urine sugar makes the patient conscious of overeating in terms of the quantity and the type of the food. A moderately glycosuric patient under constant medical supervision can rarely have complications during the short period of weight reduction.

II. DIETING FOR NORMAL WEIGHT PATIENTS:

For maximum therapeutic response from oral hypoglycaemic agents, it is essential to reduce a few pounds of body weight in order to lower the metabolic requirements of insulin; for insulin requirement is proportional to body mass. Thus five to ten pounds of therapeutic weight reduction helps to maintain a better control of diabetic symptoms during treatment. In such cases, glycosuria should be controlled for 24 hours with an optimum dose of the drug, in association with frequent administration of smaller quantities of meals. The amount and type of carbohydrate allowed in diet should be such that sugar does not

appear in urine in a patient with normal renal threshold.

III. DIETING FOR UNDERWEIGHT PATIENTS :

As the underweight and wasted diabetic patient is in a state of acute decompensated energy metabolism, the quantity of endogenous insulin produced by sulphonylureas will perhaps not be enough, and the response might be delayed for a few weeks. One should start with an adequate dose of a biguanide to stop glycosuria and complement this with a moderate amount of chlorpropamide till adequate response is evident. Insulin could be used in the event of emergency, but it should be stopped as soon as the patient starts gaining weight and improves clinically. Patients who are not adequately controlled with only insulin, improve by addition of chlorpropamide and soon they could be put on chlorpropamide alone. Patients who are not controlled with 50-150 units of insulin do so with 100-200 mg. of chlorpropamide in course of a month. Clinical remission of diabetes is neither early nor easy with them. These patients have to be maintained on drugs and to remain slightly underweight throughout their life. Divided meals, or taking small amounts of food at frequent intervals, help to control glycosuria and to gain weight with smaller doses of drugs.

THERAPY WITH NON-HORMONAL AGENTS

I. CHLORPROPAMIDE :

Dose for dose, chlorpropamide is at least twice as potent as tolbutamide during the initial four hours of its administration to diabetics as well as to normal humans (Resster, 1957). Its hypoglycaemic action during initial 24 hours is up to 6 times greater than tolbutamide and lasts at least up to 72 hours, while tolbutamide has no effect after 24 hours (Forsham *et al.*, 1959 ; Hills and Abelove, 1959). Hence, intermittent use of chlorpropamide has been found to be possible by many workers (Fuleihan and Plimpton, 1959). It is rapidly absorbed from the intestines and its blood levels are somewhat proportional to the dose. Its blood levels of 150-175 μg. per ml., which can be achieved by the dose of 500 mg. per day, are found to be adequate for stimulation of islet cells (Beaser, 1960). Its secondary failure is very rare, and is probably due to the fact that unlike tolbutamide it is not oxidised within the organism into inactive products. Hence, it is very useful in tolbutamide failure cases.

The action of chlorpropamide is considered to be due to the production of endogenous insulin (Schneider *et al.*, 1959) and the hypoglycaemic response is believed to be proportional to the state of islet cells. Sometimes hypoglycaemic response is delayed up to 4 to 6 weeks. This is mostly seen in untreated patients with severe symptoms or complications (Canessa *et al.*, 1959). How it stimulates islet cells and how it promotes their growth and how it produces endogenous insulin are not very clear. But as with all other sulphonylureas, its definite stimulating effect has been established and clinical remission in humans (Burrell *et al.*, 1959 ; Loubatieres, 1959, 1960) and clinical cure in animals have been demonstrated. Its long acting nature is an advantage over tolbutamide, because it provides a stimulus which achieves the physiological continuity of endogenous insulin secretion. Its extrapancreatic effects are also reported, but its hypoglycaemic action in pancreactomised animals or humans might be due to some interference with the enzyme systems, because it is attended with other symptoms. Danowski and Mateer (1959) considered its immediate hypoglycaemic action to be mainly due to inhibition of gluconeogenesis in liver rather than the production of endogenous insulin ; though they also considered the latter effect to be present on prolonged therapy. Increase in the glycogen content of liver is also reported by Schneider (1959).

In comparison with tolbutamide, LD 50 of chlorpropamide, weight for weight, is somewhat higher but if its usual dose of 500 mg./day is not exceeded, toxicity remains very low. Due to the individual idiosyncrasy of the patients, only rare instances of jaundice and skin reactions are noticed (Schneider, 1959). Jaundice is definitely of cholecystic type, and the chief finding in liver function tests is the elevation of serum alkaline phosphatase. Chlorpropamide is not contra-indicated during hepatitis. According to Heinsen (1959) "not only that hepatic damage need to be feared with chlorpropamide, but also that existing hepatic damage can heal during chlorpropamide treatment". Knick (1959) mentioned that "in rats with liver damage experimentally induced by thioacetamide, chlorpropamide like other antidiabetic substances, exhibit a liver protecting action". Side effects are many but are more frequently seen with higher dosage. Most of them are transient and disappear on discontinuation of therapy or often by lowering the dose. No deaths have been proved due to chlorpropamide ; though in a few deaths improper medical care has been suspected during its toxic reactions. During necropsy examination of these patients, the essential feature of sulphonylurea treatment noticed was mild to severe lipomatosis of pancreas, the physio-

logical influence of which is very difficult to explain (Seidler *et al.*, 1958).

A question has been raised whether the continuous stimulation of beta cells may not finally bring about their exhaustion and an aggravation of diabetes! Bradley (1959) citing his experience of many thousand diabetics at the Joslin clinic states: "this potential disadvantage of these oral agents has not thus far been supported by laboratory or clinical observation". Even in the failure of sulphonylurea therapy, deterioration in the beta cell growth and function has not been reported clinically or experimentally.

Chlorpropamide was tried on 75 patients who were either untreated, or treated with insulin or tolbutamide (Table 1). The patients have been divided into 3 groups: Group 1 includes mild diabetics stabilised on around 100 mg. of chlorpropamide; Group 2 includes stable diabetics requiring 200-400 mg. daily; Group 3 includes unstable diabetics in whom a maximum of 500 mg. dose sometimes could not achieve perfect control in maturity onset type of diabetes (Table 2).

II. BIGUANIDE THERAPY:

Biguanide therapy is now considered as an adjuvant to sulphonylurea or insulin therapy. We have used it successfully in uncontrolled juvenile type or in maturity onset type of diabetes which could not be controlled with chlorpropamide therapy, due to metabolic stress. Juvenile patients require a steady and high dose (150-200 mg.) of DBI together with small doses of insulin, while the other group required a smaller amount (less than 100 mg.) of DBI till the stress period was over. Patients who were well controlled with chlorpropamide, could not tolerate DBI, and such patients who required DBI during stress period showed the symptoms of intolerance when they were again controlled with chlorpropamide. It was also found to be an excellent adjuvant to chlorpropamide in untreated patients, till they responded to it.

DBI is a potent hypoglycaemic agent with peculiar metabolic effects. It should be reserved for certain stress conditions or during delay period to chlorpropamide response in maturity onset type of diabetes. Because, slightest overdosage of the drug produces gastrointestinal symptoms, and because there are many chances of starvation ketosis, its dose adjustment demands very careful judgment.

In contrast to DBI, N'N' dimethylbiguanide or 'glucophage' has its peculiar metabolism but no ketogenic effect. Hence, it is much better tolerated and its use is advocated in hypoglycae-

TABLE 1—ANALYSIS OF CHLORPROPAMIDE THERAPY IN MATURITY ONSET TYPE OF DIABETICS

	No. of cases
Duration of treatment:	
1 month	21
3 months	15
6 months	17
1 year	15
Control:	
Excellent	50
Fair	6
Improved	9
Poor	3
Deteriorated	0
Symptomatic relief:	
Immediate	52
1 week	9
Non-symptomic	7
Response:	
1 week	52
2 weeks	10
3 weeks	2
4 weeks	4
5 weeks	0
Weight gain:	
Desirable	7
Undesirable	2
Weight loss:	
Desirable	16
Undesirable	0
Steady weight:	
Desirable	22
Undesirable	21
Diet:	
Free	29
Moderate	26
Weight-reducing	8
Self-induced	4
Imposed dieting	1
Reactions:	
Hypoglycaemic	6
Gastrointestinal	1
Skin rash	1
Complications	None
SUCCESSFUL NON-HORMONAL THERAPY	
Normalisation of metabolism:	
Remission	4
Intermittent use	16
Improved control of glycaemia in previously treated patients	50
Improvement in diabetic symptoms	68
Tolbutamide failures	18
Tolbutamide treated	10
Insulin failures (hypoglycaemic reactions etc.)	3
Insulin treated	28
Untreated	9
DETERIORATION ON LEAVING CHLORPROPAMIDE THERAPY	
Scrotal abscess on insulin therapy after leaving chlorpropamide during viral hepatitis	1

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mia-susceptible arteriosclerotic diabetics in whom sulphonylureas and insulin are contra-indicated. It has been seen to cause a very marked reduction in insulin dosage and improved control in ketotic, insulin resistant diabetics. A juvenile ketotic insulin resistant diabetic who could not be improved much with 300 units a day for 2 weeks, was controlled very nicely with 3 g. of glucophage within a week on 60 units of insulin (which could be the probable requirement for juvenile metabolism during stress). Even in severe diabetics, its insulin-sparing action sometimes allows us to reduce insulin dose by 6-8 units from over 100 units, and to omit the minimum requirement by sulphonylureas through stimulation of existing islet cells.

TABLE 2—SHOWING GROUPING OF ALL DIABETICS ACCORDING TO THE SUGGESTED THERAPY AND OTHER SALIENT FEATURES

(A) MATURITY ONSET TYPE :	
1. *Mild*	
Symptomatic or non-symptomatic	1. Insulin never constantly needed. Chances of remission 2. Excellent control with low chlorpropamide dosage on weight reducing diet, than with insulin 3. Cannot tolerate biguanides 4. Never go in ketosis 5. Complications like skin eruptions only.
2. *Stable*	
Symptomatic or non-symptomatic	1. Poor control on previous insulin up to 150 u./day 2. Excellent control with moderate chlorpropamide dose on adjusted diet 3. Cannot tolerate more than 50 to 75 mg. DBI 4. Do not go in ketosis even without treatment 5. Complications like arteriosclerotic disease and neuropathies
3. *Unstable*	
Mild and stable types during stressed metabolism	Can be controlled on addition of biguanides or insulin
Advanced diabetes with complications	1. Insulin or biguanides are necessary with high dose of chlorpropamide 2. Rarely ketotic
(B) GROWTH ONSET TYPE :	
(a) Stable on DBI or insulin	1. Less than 25 u./day 2. Rarely ketotic 3. Require 100-200 mg. DBI
(b) Stable on DBI and occasional insulin	
(c) Unstable on insulin; improved by addition of biguanides	1. Poor control with even large amounts of insulin alone (more than 25 u. insulin 2. Frequently ketotic.

Chlorpropamide is preferred for maturity onset type of diabetics because of its pancreatropic action which regulates metabolism physiologically. Loubatieres (1960) has experimentally proved that even one-tenth of the surviving islets could produce enough insulin to regulate energy metabolism. One ought to be more hopeful about the existence of islet cells and about their chances of better growth and functioning. The addition of biguanides to chlorpropamide can be justified for better control in difficult cases. We, however, doubt if its combined therapy with insulin could be of much benefit. The poor results in our hand might be due to blocking effect of exogenous insulin over islet cells. In very brittle diabetics, insulin should be supplemented with biguanides or p-oxypropiophenon, and not with chlorpropamide, till minimum insulin requirements have been reached for smooth control. At present, we can group non-hormonal hypoglycaemic agents as follows :

(a) *Pancreatropic* — Insulin-producing sulphonylureas.
(b) *Glycolytic* — Insulin-sparing biguanides.
(c) *Antidiabetic* — Insulin-protecting p-oxypropiophenon.
(d) *Non-specific* — like salicylates.

COMMENTS

One should consider diabetes mellitus as a disorder of 'energy metabolism' rather than one of only carbohydrate metabolism (Brody, 1945). Though endocrine secretion of pancreas has always been suspected to be at fault in diabetes, we could clarify little of the complicated, interdependent processes of various organs and enzyme systems involved in this disturbance of energy production, conversion and storage. Insulin has been widely utilised since its discovery about four decades ago. But in what cases, how far, and in what manner it should be utilised was never questioned, in spite of unfavourable results in a large proportion of patients comprising of so many stable maturity onset type diabetics. This was because there was no substitute for insulin, except diet control and weight reduction. We have seen that gradual increase in requirements of insulin together with increasing glycosuria, and other symptoms and dermal complications in mild

diabetics, can be better controlled with diet and weight reduction. Practically no work has been carried out on the 'gradual increasing dose' phenomena of insulin in maturity onset type of diabetics who are better controlled by small doses of chlorpropamide. We have found that the growth onset insulin deficiency diabetics (juveniles) or pancreactomised humans are stabilised on much lesser amounts of insulin than in many maturity onset type of diabetics. Hence exogenous insulin administration may not be as good as endogenous hormones, due probably to antagonistic factors like glucagon, insulinase, other hormones and also due to its blocking effect on insulin production. All diabetics do not lack islet cells and pancreatic insulin (Wrenshall, 1960) ; but we know little about what happens to such large amounts of injected insulin in mild diabetics. It is known that normal animals could be made temporarily diabetic on severe carbohydrate restriction diet and insulin injections (Haist, 1960). We do not take as much precaution with insulin as we do in the administration of steroids and other hormones. But future research may prove insulin to be like all other hormones, and may not justify its regular use in the treatment of diabetes, except in real deficiency states ; because we have not yet discovered a non-hormonal agent which could take over all the physiological functions of insulin. Even during emergencies like ketosis, we see great utility of insulin sparing action of glucophage and pituitary inhibiting action of p-oxypropiophenon. We may regard large insulin requirements of many diabetics to be due to something else than for real metabolic requirements ; and accept insulin producing, insulin sparing or protecting non-hormonal agents as preferable to insulin injection in most of the diabetics.

Much better metabolic regulation has been seen with new oral agents in patients who were either tolbutamide failures or were unhappy with insulin therapy. So, we propose a term 'non-hormonal therapy' for the treatment of diabetes with the existing oral hypoglycaemic agents, and try to establish definite indications of 'non-hormonal therapy' with such oral preparations and 'hormonal therapy' with insulin in various types of diabetic conditions.

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CASE NOTES

CHORIONEPITHELIOMA

With Unusual Features

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The recent interest created by the pathological entity of chorion epithelioma is universal. A number of gynaecologists and gynaecological pathologists from all over the world have discussed its various aspects. This widespread interest is due to its variance of incidence in different countries, multiplicity of clinical features, difficulty in histological diagnosis, associated hormonal status of the patient, and the problem of appropriate surgical management.

Tracing back the history of medical research, we find that the malignant nature of a growth associated with hydatidiform mole was first described by Gregorini (1795). His patient developed metastasis in the lungs following a molar pregnancy. Since then, only sporadic reports (Volkman, 1867; Sanger, 1889) are available until hundred years later, when an epoch making study by Marchand (1895a, 1895b, 1898) determined the true nature of the growth from trophoblasts. The first attempt of pathological correlation with clinical features was made by Ewing (1910) when he designated three different grades of the disease as syncitioma, chorioadenoma destruens and choriocarcinoma. The problem of chorionepithelioma is more important in Eastern countries due to its greater incidence rate (Acosta-Sison, 1949; Hooper, 1955), and as such any discussion on this subject is worthwhile.

In the present paper two interesting cases of chorionepithelioma are presented.

CASE REPORTS

CASE 1—I.M., aged 22 years, was admitted on 4.8.57 at 10 A.M. with the following complaints: History of fainting attack—1 day. Acute pain in the lower abdomen associated with slight bleeding per vagina preceding the fainting attack—1 day.

Obstetric history—Pregnancy—1. Abortion—1, at 16 weeks (molar pregnancy)—9 months back.

Menstrual history—Menarche—at 13th year; cycle 28±2 days; duration, 4-5 days; regular. Last menstruation—1.7.57.

History of present illness—The patient aborted spontaneously at 16th week of gestation about nine months back, which was diagnosed to be a molar pregnancy. No definite history of postabortal curettage was available. She started her normal period in January 1957, which continued upto April 1957 at regular intervals. After that the periods became profuse and prolonged, but still cyclical. For this complaint she had endometrial curettage in July 1957 in a local hospital, but the pathological report could not be obtained. On 3.8.57 she experienced acute pain in the lower abdomen with slight bleeding per vagina, followed by fainting attacks. Fluid transfusions and resuscitative treatments were carried out at patient's house with no improvement in her condition.

Condition on admission—The patient was admitted in a state of shock, with pulse rate of 140 per minute, regular and of low volume and tension. Respiration was 30 per minute, regular. Blood pressure was S/D−104/58 mm. of Hg. Sublingual temperature was 101°F. The patient looked severely ill and grossly pale.

Systemic examination revealed no abnormality.

Abdominal examination—Extreme tenderness was elicited in the left iliac and hypogastric regions. Shifting dullness was present. No lump could be felt. There was generalised meteorism.

Pelvic examination—Scanty serosanguinous discharge was visible. Uterus was in mid-position, slightly bulky, a little soft in consistency. Pouch of Douglas and both culs were tense in feel and markedly tender on superficial palpation. No definite lump could be recognised.

Investigations—Hb.—3·7 g. per cent. E.S.R.—49 mm/1st hour.

Management—The diagnosis being disturbed ectopic pregnancy, immediate laparotomy was decided upon. After opening the abdomen, the peritoneal cavity was found to be full of blood. The tubes and ovaries were found to be normal. The uterus was bulky and on its posterosuperior aspect there was a purple coloured growth of about one inch diameter, with areas of dehiscence of the uterine muscle over it. Blood was found to be oozing out from it. Suspecting it to be a case of chorioadenoma destruens, a total hysterectomy was performed. During the operation the patient received a pint of whole blood and a pint of 5 per cent glucose saline was continued in the post-operative period. She was behaving well, but six hours after operation she suddenly developed pulmonary oedema and expired.

The specimen showed spontaneous perforation on the posterior aspect of the uterus (Fig. 1).

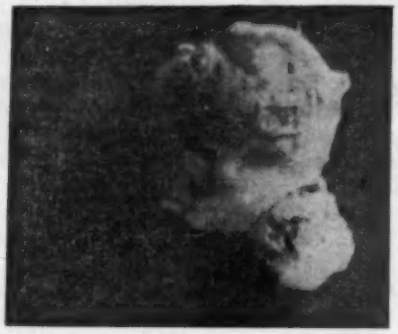

FIG. 1—SHOWING THE UTERUS FROM ITS POSTERIOR ASPECT. THE AREA OF SPONTANEOUS PERFORATION ON ITS WALL IS SEEN (CASE 1)

Histological report—(a) Superficial haemorrhagic spot—The section revealed infiltration of the myometrium with chorionepithelioma, the cells being mostly of cytotrophoblastic type (Fig. 2, *vide* Plate). (b) Posterior surface of the uterus—Similar picture with invasion of blood vessels. (c) Haemorrhagic spot on the cervix—Signs of chronic inflammation with localised superficial haemorrhage.

Unfortunately, the permission for holding a post-mortem examination was not obtained, and so evidences of visceral metastasis could not be determined. Hormonal estimation of urine was also not feasible as the patient died very early.

CASE 2—K.S., aged 20 years, married for 10 years, was admitted on 7.8.60 with the following complaints: Irregular bleeding per vagina for 8 months, profuse in quantity for the last four days. Something coming down per vagina—1 month. Weakness of the lower limbs—4 days.

Obstetric history—No. of pregnancy—3, living—1. First pregnancy—at the age of 14 years; twin pregnancy; at 32nd week both born dead. 2nd pregnancy—at term, living and healthy—5 years back. 3rd pregnancy—abortion at 16th week—4 years back.

Menstrual history—Menarche—at the age of 11 years; cycle—28±5 days; duration, 2-3 days, scanty, irregular. Last menstruation—could not give accurate history, probably nine months back.

History of present illness—The patient was having irregular bleeding per vagina for the last eight months, with absence of cyclical bleeding. About a month back she noticed a mass coming out per vagina which bled to touch with the clothings and during ablutions. For the last four days she was having occasional profuse bleeding per vagina which made her very weak. She also noticed severe pain during movement of the lower limbs for the last four days.

Condition on admission—The patient was admitted in a state of shock with blood pressure of S/D=90/60 mm. of Hg and a thready pulse, rate being 156 per minute. The patient looked extremely pale and severely ill. Sublingual temperature was 100°F.

Systemic examination—Heart—no apparent abnormality. Lungs—few areas of diminished breath sounds in both lung areas. Liver and spleen—not palpable. No mass could be felt per abdomen. A tender area was located in the right femur about 5" below the greater trochanter.

Pelvic examination—Serosanguinous discharge, moderate in amount, was visible.

A fungating, haemorrhagic, and friable growth of the size of a small orange (2 inches × 2½ inches) was observed attached by a broad base, originating from the anterior vaginal wall, just from the inner aspect of the left labium minus (Fig. 3). A small cystic growth was found to originate from the similar site on the right side.

Uterus—slightly bulky, firm and anteverted. Cervix—smooth and apparently healthy. Culs—bilateral tender cystic lumps palpable.

Investigations—Blood (7.8.60): Hb.—5·4 g. per cent. R.B.C.—1·6 million/c.mm. Leucocytes—6,800/c.mm. Neutrophils—76 per cent. Lymphocytes—20 per cent. Monocytes—4 per cent. E.S.R.—60 mm./1st hour.

Hb. (25.8.60)—2·6 per cent.

FIG. 3—SHOWING THE VAGINAL GROWTH. A RUBBER CATHETER IS SEEN INTRODUCED INTO THE URETHRA (CASE 2)

Urine—Reaction—acid. Albumin—trace. Pus cells—plenty (12 per field on an average). Urinary chorionic gonadotrophin estimation (by male toad test) showed that the hormone titre was not less than 12,50,000 units/litre of urine which was highly suggestive of chorionepithelioma (Report by Dr. Lahiri. Department of Zoology, University of Calcutta).

Skiagram of chest, pelvis and femora—Metastatic malignant shadows seen in both lung fields but no abnormality in pelvic bones and femora.

Management—On admission the patient was resuscitated with 5 per cent glucose saline transfusion and one pint of Gr. 'O' Rh+ve whole blood. Broad spectrum antibiotic was given intramuscularly every six hours. Crude liver extract and iron were administered. The temperature came down to normal within a week, but otherwise, the general condition of the patient gradually deteriorated. Slight vaginal bleeding from the growth persisted. Another pint of whole blood was transfused. The patient became restless very often from 20.8.60 and sedatives had to be administered occasionally. The patient had a severe bout of haemorrhage from the vaginal growth on 25.8.60, collapsed and became dyspnoeic. In view of the persistence of haemorrhage from the vaginal growth it was removed under local anaesthetic (xylocaine 2 per cent). Another pint of whole blood was administered with concomittant prednisolone and noradrenaline therapy, but the patient expired the same day.

Post-mortem examination—The uterus with its appendages and the vagina and vulva were removed as a whole (Fig. 4).

FIG. 4—SHOWING THE UTERUS, VAGINA AND THE APPENDAGES. A GROWTH IS SEEN IN THE FUNDUS. OVARIES ARE CYSTIC. A METASTATIC NODULE IS SEEN AT THE LOWER PART OF THE VAGINA (STRETCHED BY A GLASS ROD). (CASE 2)

Kidneys—normal. Liver—normal. Lungs—multiple metastatic nodules in both the lungs. Brain—normal.

Histological examination:

(a) Material from the body of the uterus with the growth showed typical choriocarcinoma consisting of both types of cells with haemorrhage and muscle destruction. (b) Those from the vaginal growth and the metastatic nodules on the inner side of the right labium minus—same features as above. (c) Those from the metastatic nodules in the lungs showed destruction of lung parenchyma by both types of malignant chorionic cells with haemorhage.

DISCUSSION

The importance of trophoblastic growth has been emphasised by the creation of Mathien Chorionepithelioma Registry in the United States.

As mentioned previously the incidence of molar degeneration of trophoblast is common in eastern countries and as such reports from our hospitals present varieties of peculiar clinical features of this disease.

With a typical history of persistent sanguinous vaginal discharge following a molar pregnancy (after a variable interval), wasting, cough, haemoptysis and a rising titre of urinary chorionic gonadotrophin, the diagnosis of chorionepithelioma becomes easy, but difficulty arises in cases with atypical clinical features.

The first case was admitted with a history typical of disturbed ectopic gestation. The urgency of the case necessitated early laparotomy which revealed a typical perforating chorioadenoma destruens. Being a young girl both the ovaries were kept intact and total hysterectomy was performed but she succumbed to pulmonary oedema which led to the suspicion of pulmonary metastasis of a chorionepithelioma. Autopsy examination was not allowed but histological examination of the uterus revealed a typical chorionepithelioma. Rarely has a case of chorionepithelioma with similar clinical features been reported.

The second case had all the clinical features of a typical metastasising chorionepithelioma and was admitted in a moribund state. She could not be revived for extensive surgery and the vaginal growth only was excised to remove the source of persistent haemorrhage. The interesting feature of this case is the latent interval of four years between the last known pregnancy which ended in abortion and the development of chorionepithelioma. The usually accepted interval is not more than one to two years. This feature, though unusual, is not unknown (Brews, 1950; Medina and Salvatore, 1951; Limburg, 1952; Bevis, 1954). It is an accepted fact that chorionepithelioma might follow any type of pregnancy. Amongst the cases of Smalbraak (1957), 47 per cent were preceded by term pregnancy, 38, per cent by molar pregnancy and 23 per cent by abortion. The recent contention of noted

pathologists all over the world is that about 40 per cent of early abortions are associated with molar degeneration of trophoblasts, which can only be established by routine histological examination of all abortions. The second case reported had a history of abortion about four years back. It is not improbable to conceive that there might have been unrecognised hydatidiform degeneration of trophoblast in that pregnancy.

Summary

Two interesting cases of chorionepithelioma have been presented. The first case simulated the clinical features of a typical disturbed ectopic gestation and the second followed an abortion after a long interval of four years, both terminating fatally.

Acknowledgment

The authors are grateful to the Superintendent, R. G. Kar Medical College Hospitals, Calcutta, for permission to publish the case records.

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NORMALISATION OF CARBOHYDRATE METABOLISM IN MATURITY ONSET TYPE OF DIABETES

S. K. MUKHERJEE, M.SC., M.B.B.S. D.PHIL.

AND

S. S. MUKHERJEE, M.B.B.S.

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Clinical reports on various degrees of control of diabetes mellitus with sulphonylureas (Dolger, 1959, Mohnike and Stotter, 1956; Granville-Grossman *et al.*, 1959) are available. Normalisation of glucose tolerance or its improvement caused by sulphonylureas in course of drug administration has been recorded in a few instances (Talpers *et al.*, 1957; Tornow *et al.*, 1959; Fajans are Conn, 1960). It is known that adult diabetics respond favourably to dietetic treatment (Bloom, 1959).

In course of screening of oral antidiabetic compounds we have come across two cases (Cases 3 and 227) of maturity onset diabetes (clinically), whose response to treatment seemed interesting. These cases are reported.

Case Reports

Case No. 3—A male, 42 years of age, suffering from diabetes mellitus for about 6 months was treated by diet only. The disease started with polyuria, polydipsia, etc. He is a technician, eating a mixed diet, and having a normal body weight. There was no family history of diabetes. He was put on the usual diet (carbohydrate 200 g., protein 0·8 g/lb. body weight and fat to make up the remaining calories, calculated from height and age). He was simultaneously prescribed a placebo for 60 days during which his blood and urine sugar were repeatedly checked to confirm his diabetic condition and ascertain improvement, if any. After the 60th day the placebo was omitted but the diet maintained.

Case No. 227—A male, aged 51 years, suffering from diabetes for about two months was treated by dietary regimen only. The disease started with polyuria, polydipsia, etc. He was a technician, eating a mixed diet and having a normal body weight. There was no family history of diabetes. A standard dietetic regimen was prescribed for a period of 60 days, during which his blood and urine were repeatedly checked for sugar to confirm his diabetic condition and to assess improvement, if any.

Subsequently he was treated with chlorpropamide as follows: 1st day 2 g., 2nd day 1·5 g, 3rd day 1·5 g., 4th to 7th day 1 g. and 8th to 21st day 0·50 g. daily. Then the drug was withdrawn and the patient was instructed to maintain the diet prescribed for him.

In both the cases oral glucose tolerance tests (50 g. glucose) were done. Blood sugar was estimated by Folin and Wu's method periodically for 18 months in case no 3 and 19 months in case no. 227 after withdrawal of the drug (Fig. 1).

Discussion

We have recorded two clear-cut cases of diabetes mellitus clinically belonging to maturity onset type of diabetes showing considerable metabolic remission on

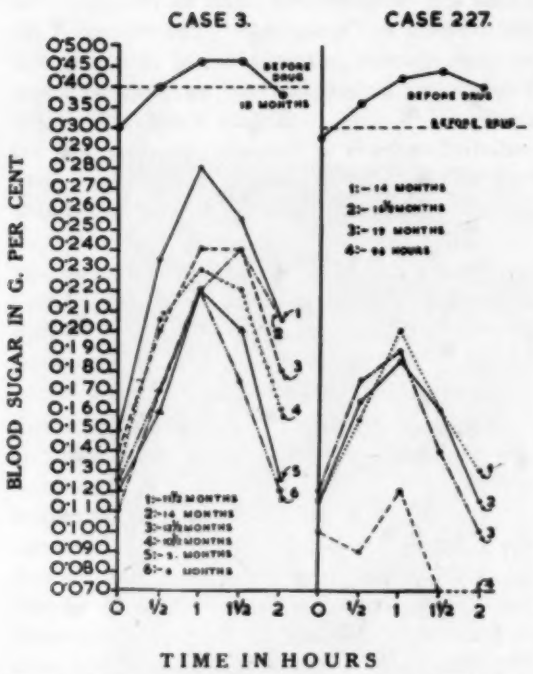

FIG. 1—SHOWING ORAL GLUCOSE TOLERANCE CURVES IN THE REPORTED CASES BEFORE AND AFTER CHLORPROPAMIDE

TABLE 1—SHOWING WEEKLY READINGS OF BLOOD AND URINE SUGAR BEFORE, DURING AND AFTER CHLORPROPAMIDE THERAPY IN THE REPORTED CASES

Time (weeks)	Case 3		Case 227	
	Blood sugar (mg.%)	Urine sugar (g.%)	Blood sugar (mg.%)	Urine sugar (g.%)
	BEFORE DRUG THERAPY			
First visit	400	4	300	5
4	...	...	310	4
9	...	...	310	4
	DURING AND AFTER DRUG THERAPY			
2	230	1·2		
3	...	...	100	nil
4	135	nil	...	
6	130	nil	...	—
9	140	nil	...	

treatment. Case no. 3 relapsed within 18 months although he adhered to his prescribed diet. Subsequently the disease was controlled by tolbutamide. This can be considered as a case of spontaneous remission of the disease as observed by other workers (Peck *et al.*, 1958; Stutman and Hayes, 1959; Waddell, 1959; Harwood, 1957; Taylor, 1960).

Improvement in glucose tolerance after chlorpropamide therapy in case no. 227 (Fig. 1) must be due to the effects of chlorpropamide and diet. This corroborates earlier observations (Talpers *et al.*, 1957; Tornow *et al.*, 1959; Fajans and Conn, 1960). That withdrawal of antidiabetic drugs causes recurrence of the diabetic condition is well known. Judging from fasting blood sugar or urine sugar levels (24 hours), shown in Table 1, case no. 227 was very near to normal during and after withdrawal of chlorpropamide. Glucose tolerance patterns noticed periodically for 19 months after withdrawal of chlorpropamide was also near normal range. Maintenance of metabolic pattern in a normal level in this patient cannot be due only to dietary regime as it had earlier failed to evoke much change in the blood or urine sugar levels before instituting chlorpropamide therapy. Failure to maintain case no. 3 in a normal metabolic state by diet alone indirectly supports our contention.

The exact mechanism and site of action of the sulphonylureas are not known but its effect on the β cells of the pancreatic islets is firmly established. It can be postulated that chlorpropamide alters the activity of endogenous insulin in maturity onset type of diabetes thus showing its normalising action on carbohydrate metabolism in case no. 227.

ACKNOWLEDGMENT

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POLYPEPTIDES AFFECTING SMOOTH MUSCLES AND BLOOD VESSELS

Modern knowledge in biological science is incomplete without proper appraisal of polypeptides. Antibodies, antibiotics, enzymes, most hormones and many other active substances of biological importance are composed of polypeptides. Amongst these, some are cyclic in nature with amino acids of dextro configuration and others contain laevorotatory amino acids. Antibiotically active peptides and peptide hormones of anterior pituitary contain dextrorotatory amino acids whereas vasopressin, oxytocin, hypertensin and some others contain laevorotatory amino acids.

Posterior pituitary hormones, mainly oxytocin and vasopressin, at present can be studied for their biological activity and, if available in the purest form, for their biological assay also. Their chemical structures were not known to us before 1953, when Du Vigneaud *et al.*[1] in U.S.A. and Tuppy[2] in Austria simultaneously suggested a formula and established their chemical structures to make synthesis possible thereafter. Difficulties are still present for biological assay of the two posterior pituitary hormones. Many methods of biological assay have been described but none of them are absolutely specific, the chief obstacle being that highly purified natural or synthetic vasopressin or oxytocin are very difficult to preserve as a standard; for example, if oxytocin is kept in powder form di- or polymerisation occurs. Maximum stability can be obtained for both the synthetic and naturally occurring product in solution form at *p*H 3. There is a good correlation between the structures of posterior pituitary hormones and their pharmacological actions and of their analogues. There are two separate enzymes, oxytocinase and vasopressinase which *in vivo* inactivate the oxytocin and vasopressin. The activity of the enzymes is much increased during pregnancy and a convenient method has been established for estimating oxytocinase. Clinical significance, application of oxytocin in obstetric procedure, and the role of oxytocin in uterine inertia have been revealed. Recent studies by cardiac catheterisation (collecting blood from internal jugular vein) and other methods show that the oxytocic activity is in a much higher concentration in central than in peripheral blood, an observation which evidently shows that active substances in the extract are of neurohypophysial origin.

Angiotensin is another polypeptide which is also comprised of l-amino acids characteristic of ordinary proteins, a globulin factor, with vasoconstrictive effect. In 1898 Tigerstedt first noticed the influence of kidney cortex upon circulation. In 1936 Pickering[3] and others confirmed the findings of Tigerstedt and Bergman's work. Before this 'renin' did not find any place in the textbooks of physiology. In 1949 Page[4] noticed that renin reaching the blood plasma produced a new substance having new properties. Braun-Menendez[5] called it 'hypertensin', Page called it 'angiotonin'. In 1958 physiologists agreed to accept the name of angiotensin. The method of obtaining angiotensin in large quantities has been established. Study and assay of the angiotensin in various hypertensive diseases have been done by various workers. Kahn *et al.*[6] in 1952 assayed the angiotensin in normotensive subjects and in essential hypertension and also in the malignant group. They noticed that the average angiotensin content in normotensive subjects was 0·015 unit per litre and in the malignant group 0·3 unit per litre (almost 20 times higher). In 1954 Skeggs *et al.*[7, 8] noticed that if angiotensin is injected to normo-

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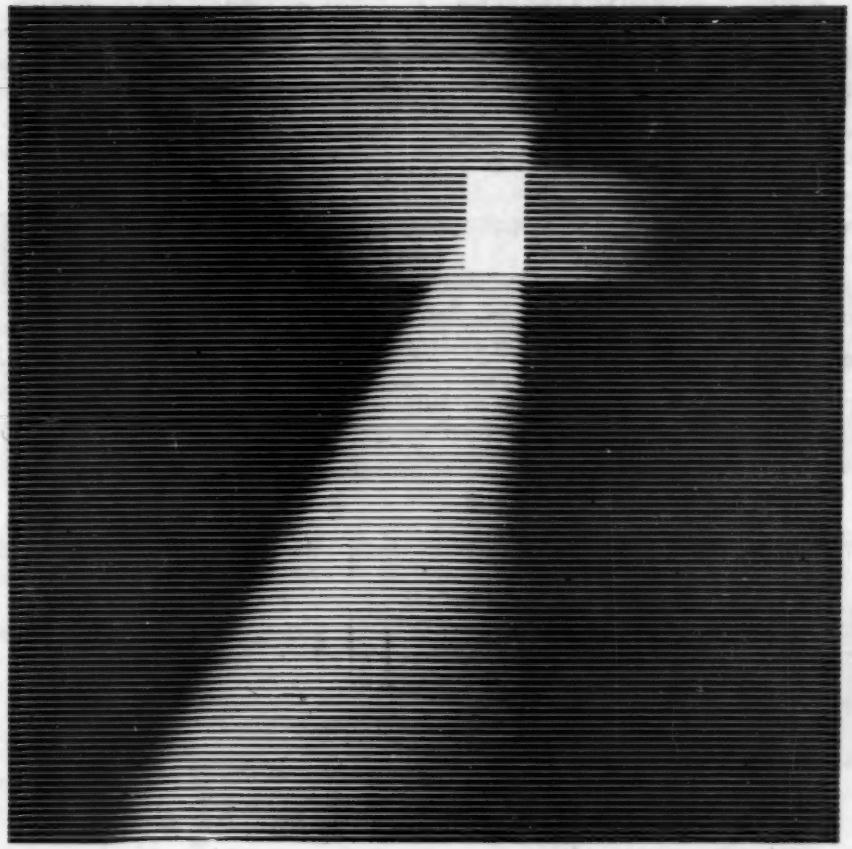

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tensive subjects it can raise the diastolic pressure by 40 mm.Hg and remain persistent for 10 minutes and the concentration of angiotensin in serum is about 0·3 unit per litre. These observations establish the renin-angiotensin systems and their role in hypertension. These authors have also studied the detailed pharmacological action of angiotensin and compared it with that of noradrenaline. The most interesting thing they have noted is that hydralazine which decreases the response of arterial wall to vasoconstrictive substances did not influence the effect of hypertension in dogs. Though much has been said about renin-angiotensin pressure system the exact site of renin formation is still a mystery. Cook and Pickering[9], by fragmentation of cortex containing emboli of iron oxide and separating these portions by electromagnet, concluded that renin is contained in a structure close to glomeruli. Skeggs *et al.*[10] demonstrated that angiotensin is the cause of hypertension, but Peart[11] differs from them and according to him renin and angiotensin cannot be the sole cause of hypertension.

In 1931, Euler and Gaddum[12] noticed that extract of some tissues contained a peptide and they termed it 'substance P', which is found in the intestine, brain and retina. They found that 'substance P' of the intestine differs from that of the brain in pharmacological action in several dysfunctions of C.N.S., such as sedation or stuporous condition in cats, increased respiratory activity in cats and rabbits, hyperalgesia in mice, interruption in morphine-induced analgesia in mice, stimulation of morphine depressed respiration and anticonvulsive action against strychnine in mice. But the main task about 'substance P' is to establish a formula for it. It is for the biochemist to suggest and establish its formula.

Other members of the group of polypeptides which affect smooth muscles are kinins—tissue kinin, urinary kinin and blood kinin. Blood contains a substance called kallikreinogen, a precursor of kallikrein and it has also been demonstrated that blood contains an enzyme which destroys kallidin. Bradykinin was extensively studied and described by Rocha e Silva[13] in 1948, but still it is not clear whether bradykinins and kallidin are the same substance or not. It is reasonable to consider that they are similar substances and may be called 'kinins'.

The role of polypeptides and their importance have further been extended to the study of the causation of anaphylactic shock (due to anaphylotoxin, a globulin) and of inflammation by the polypeptide, leucotaxin, and the nucleoprotein, exudin. It is known that anaphylactoxin of Friedberger[14], who postulated the humoral theory in anaphylactic shock, is a histamine liberator and also that histamine is found in inflammatory exudates. Much of the changes in blood vessels and capillaries, both in inflammation and anaphylactic shock, simulate those due to histamine or histamine liberation. But the difficulty lies in the fact that animals like the rat, which never liberates histamine in anaphylaxis, suffer from anaphylactic shock. This hypothetical substance which is most probably a proteinous substance has not yet been demonstrated—whether it is an enzyme, a probable protein activator or the product of some enzymatic activity. The changes in the blood vessels and in the permeability of the capillaries in inflammation, could not be shown to have any relation to the content of histamine in the inflammatory exudates. Intensive study with inflammatory exudate has, however, revealed recently that it contains two factors—exudin and leucotaxin. The latter has the capacity to cause migration of leucocytes, hence called leucotaxin, in addition to the permeability of the capillaries, whereas exudin increases only the permeability. This new knowledge of the various chemical mediators liberated in turn by injured cells in an inflamed area is opening up a new vista for further biochemical exploration of the basic immunological phenomenon of inflammation.

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PRESIDENT'S PAGE

Address at the Nilratan Sircar Centenary Celebrations

Dr. H. N. Shivapuri, President, Indian Medical Association, delivered the following address at the Nilratan Sircar Centenary Celebrations at Calcutta on October 1, 1961 :

DR. ROY AND FRIENDS,

Lives of great men all remind us
We can make our lives sublime,
And departing leave behind us
Footprints on the sands of time.

—LONGFELLOW

These oft-repeated and popular lines were never more true than in such cases as the life of late Dr. Nilratan Sircar. He has blazed a trail for all of us to follow and has left permanent footprints.

We have today gathered here to celebrate the birth centenary of one of the leading physicians the country has produced during modern times.

The year 1861 was, it seems to me, specially lucky for us—Indians—as that year saw the birth of such great men of our land as the poet Rabindranath Tagore, Acharya Profulla Chandra Roy, Pandit Motilal Nehru, Dr. Nilratan Sircar, Pandit Madan Mohan Malaviya and the great musician Vishnu Narayan Bhatkhande who modernised and resuscitated the dying Indian classical music. I hope the year 1961 will prove equally worthy, but that, of course, will only be known at least 50 years hence.

Nilratan Sircar was not only a great physician, but a person with noble emotions. He had great visions and ideals which he set about to carry out in his own characteristic way. He was a self-made man and a great patriot, who believed in self-reliance and the country being made economically self-supporting and self-contained.

It is a remarkable fact that nearly all great men have been greatly influenced by their mothers and Nilratan Sircar was no exception to the rule. In fact, if he did not love his mother dearly, he might not have become a doctor at all, but might have taken to some other profession. But it is equally certain that he would have shown as well in that profession also. There are certain persons who are born to become great and to adorn whatever avocation they may choose for their life's work and Nilratan Sircar was such a genius.

His hospitality was well known and his doors were always open to friends and strangers alike. Though he earned like a prince, he spent also like a prince, and he spent well in good causes such as advancing the cause of the industrial growth of his country, as is evident from the fact that he started so many industries. I remember to have used in my childhood and younger days soaps of the National Soap Factory as my father believed in Swadeshi and he would not purchase foreign articles, if he could get a home made article and he switched on to these soaps as soon as he learnt about them.

I will here recall that Dr. Sircar was one of the founders and main architects of the Indian Medical Association which took its birth here in Calcutta in 1928. He was one of its early Presidents, being President of the Association in the year 1931-32 and as such presided over the eighth All-India Medical Conference held at Calcutta in 1931. He was also the first Editor of the *Journal of the Indian Medical Association* and edited it for 13 long years from 1938 to 1941 and its foundation was well and truly laid by him.

He also took leading part in medical education and was Dean of the Faculty of Medicine of Calcutta University for a number of years as also Vice-Chancellor of the University (1919-1931). For the medical profession of this country he was a torch-bearer and we can do nothing better than to follow the precepts laid by him. It is for such great men that an English author, Charles Reade, wrote : "The words and works of a genius so high are not born to die. Their immediate work upon mankind fulfilled, they may seem to lie torpid, but at each fresh shower of intelligence Time pours upon their students, they prove their immortal race ; they revive, they spring from the dust of great libraries ; they bud, they flower, they fruit, they seed, from generation to generation, and from age to age."—*Jai Hind*.

Inaugural Address at the Silver Jubilee Celebrations of Barrackpore Branch, I.M.A.

Dr. H. N. Shivapuri. President, Indian Medical Association, delivered the following address while inaugurating the Silver Jubilee Celebrations of Barrackpore Branch, I.M.A., on September 24, 1961 :

MR. PRESIDENT, LADIES AND GENTLEMEN,

I thank you most sincerely for giving me this opportunity of meeting friends in Bengal again. My first acquaintance with the great city of Calcutta was in December 1926, when I was posted to Burma and passed through Calcutta. I had read and heard so much from my childhood about Bengal and Calcutta, that I had a feeling of awe before coming. Somehow in those days a feeling had grown that everyone here was a revolutionary and going about with a live bomb in his pocket or in her handbag. Those were the days when incidents like that of Sir Curzon Wylie or the bomb thrown at Lord Hardinge were not uncommon. But when my wife and I arrived in Calcutta, we met very friendly people to our great satisfaction. We stayed for two days in a Bengali Hotel and thoroughly enjoyed our visit before sailing for Rangoon.

Since then I have been frequently in Calcutta and everytime I have come here, I have had very friendly reception and experience, so much so that I am now in love with Calcutta and its people.

I have lost the count, as to how many times I have been here. In 1961 alone, this is my sixth visit and another one is in the offing next week. You will thus see that when I come to Calcutta, I come to a place which I have begun to feel like my second home.

Indian Medical Association, as compared to similar institutions in other parts of the world, is a young body having been born only in 1928 in its present form. There were some efforts before at our coming together, but these were only partially successful. But even in these 33 years of our existence, the Association has had varied experiences. We were looked upon with suspicion in the beginning as was the lot at that time of all national meetings, bodies or associations. In some provinces we were officially tabooed, in others we were looked askance at and in the remaining few we were just tolerated. We were then more or less a graduate independent practitioners' association, as in the beginning even the licentiate friends were in the other camp and basking in the official sunshine. Much water has flowed since then under the great Hooghly bridge—even the bridge itself is now in a new garb. We are now not so badly off. All classes are now our members, Government servants, licentiate friends and private practitioners. Even military officers are joining in numbers, but we are still very far from our goal of universal membership like our counterparts in U.K., U.S.A. and other advanced countries of the world. And until, ladies and gentlemen, we achieve that position, we cannot have that influence with the Government as we would like to have or as B.M.A. or A.M.A. have in their countries. Our immediate objective, therefore, should be a very large increase in our membership and a sense of discipline in our ranks.

These Annual Meetings have great value in allowing us to collect together and review our activities and giving us an opportunity to formulate new policies or changing old ones according to the needs of the time. A Jubilee is a still bigger occasion in letting us ponder on our work of 25 years and trying to follow or adapt the policies formed by our elders and judging as to how far we have succeeded in following the footsteps of our predecessors and what mark they have left and what we will leave on the sands of time when our time comes. A Jubilee is, therefore, a very happy occasion whether in the life of an individual or in that of an Association and is a matter of congratulation for having—shall I say—successfully completed 25 years of existence. It is the first 25 years that in our country occur large numbers of casualties ; our infantile mortality is the heaviest and now happily Barrackpur Branch has safely crossed that dangerous period of life.

The Secretary of the Branch—Dr. B. K. Ghosh has given you a short history of the Branch and its activities and it is a record of continued progress. I congratulate the members of the Branch on its bright record and progress.

I must specially congratulate the Secretary, Dr. Ghosh, for a fine record. I confess I had not spotted my old friend, when I saw the name in print but only when I saw him yesterday I found that he also belongs to the old gang like me. I find that he was the first Secretary and he still continues to be so. I take it that he has been Secretary all this time—an unbroken period of 25 years, a truly remarkable record of service. This also shows that he must be a person with remarkable personality to have kept the confidence of the branch for such a long and uninterrupted period.

In all this gathering I miss one person—my friend late Dr. Souren Sen Gupta—the live wire of the Bengal State Branch. A young life cut in

its prime, I have suffered a personal loss in his untimely death and I can quite understand the loss that you all have sustained. May God give peace to his departed soul!

I understand Barrackpore was the first place in the country where the first shot for freedom was fired in 1857. As the name implies, Barrackpore, at that time must have been purely a military cantonment and Barrackpore is, therefore, entitled to a golden page in our new chapter. I also understand that this place is associated with our great leader—late Surendranath Banerjee. I have heard him delivering a speech and commanding an audience of over 10,000 people in days when there were no loud speakers and amplifiers. Barrackpore for all these reasons has a record of which it can be proud, and I convey my greetings to the people of the place that they have such honourable and great precedences to follow.

Ladies and gentlemen, with the coming of Independence, a new age has dawned on our country and new problems have arisen. We of the National Medical Association and its Branches have to change our routine of work and ideas. We have to think over as to what should be the role of this Association in the building of the future of the nation and how we are to share the burden and work out the various problems of health facing us in the immediate future. It is a difficult problem indeed, but we have to think and find a solution.

In the words of Swami Vivekananda:

> The duties of life are sore indeed,
> And its pleasures, fleeting vain.
> The goal so shadowy seems and dim,
> Yet plod on through the dark, brave heart,
> With all thy might and main.

With these words, ladies and gentlemen, I congratulate Barrackpore Branch on its having completed successfully 25 years of existence and wish it a virile period of sturdy progress in future and I have great pleasure in inaugurating the Silver Jubilee of the Branch.

In the words of the great Russian writer Boris Pasternak:

> A new shower
> Through the fields is going,
> And new seeds
> In furrows he's throwing,
>
> ... ...
>
> And Time will see our hope fulfilled.

GENERAL PRACTICE DIGEST

STRESS INCONTINENCE IN WOMEN

Incontinence has been defined as the passing of urine except during the normal act of micturition. If it occurs only, or mainly, when there is a sudden rise of intra-abdominal pressure (during a cough or sneeze) it is termed stress incontinence. The underlying cause of this condition is a weakness of the internal sphincter which permits escape of urine when there is a sudden rise of pressure upon the bladder.

There are 3 causes of stress incontinence, viz., childbirth, congenital weakness of the sphincter, and injury of the sphincter by surgical operations. The first of these is most common and is most amenable to treatment.

(A) STRESS INCONTINENCE DUE TO CHILDBIRTH:

The ligaments which support the bladder and the urethra may become stretched or damaged during childbirth. The structures are no longer held up in their correct position under the symphysis pubis. Though not damaged, the internal sphincter of the bladder may not be maintained in its normal position, and it becomes ineffective and stress incontinence develops. If it occurs immediately upon delivery, a spontaneous cure often occurs within a few months. But if it develops insidiously some years after childbirth, it gradually becomes more severe.

The cause of stress incontinence is descent of the bladder neck when the intra-abdominal pressure is suddenly raised. It can be cured by restoration of the bladder neck to its former anatomical position.

The *essential* points in the diagnosis of stress incontinence following childbirth are:

(1) Normal urinary control before parturition;

(2) Incontinence occurs only when the intra-abdominal pressure is suddenly raised (e.g. on coughing or sneezing); and

(3) The incontinence can be clinically seen and prevented by supporting the neck of the bladder.

Other *additional* points in diagnosis are:

1. The stress incontinence only occurs or is much more severe when the patient is up and about, and never when she is recumbent;

2. There is increased frequency of micturition by day, but little or no nocturnal frequency;

3. Urine examination, intravenous pyelography, and cystoscopy are normal.

Special x-ray technique has been developed for demonstrating descent of the neck of the bladder.

Cystocele and descent of the neck of the bladder following parturition are independent entities. A patient with a very large cystocele may have no bladder neck descent, and therefore no stress incontinence. The following simple method of x-ray diagnosis has been devised for differentiating the above two conditions:

A balloon catheter is passed into the bladder and the balloon is filled with radio-opaque medium—this will rest upon the neck of the bladder when the patient is up-

right. The descent of the balloon and therefore of the bladder neck, can be clearly seen in films taken at rest and whilst the patient is straining.

Operative treatment—This is quite satisfactory. The bladder neck if replaced surgically to its former anatomical position will result in the internal sphincter becoming effective again and able to withstand any sudden rise of intra-abdominal pressure.

Anterior colporrhaphy will give about an 80 per cent cure of stress incontinence. The causes of failure of this operation are :

1. Technical failure to achieve replacement of the bladder neck;
2. Error in diagnosis, where the sphincter has been damaged;
3. During the operation of colporrhaphy the sphincter fibres may be damaged or immobilised by subsequent fibrosis.

Other operations have been devised for recurrent stress incontinence the basis of many of them is to 'sling' the bladder neck up behind the symphysis pubis by using a strip of fascia, cut either from the fascia lata of the thigh, or cut from the external oblique muscle of the abdomen.

The technique of Everard Williams (1947) is perhaps the operation of choice for any patient with recurrent stress incontinence following an anterior colporrhaphy. The principle of this operation is to expose the bladder and bladder neck through a suprapubic incision and to suture the bladder neck with plain catgut to its former position behind the symphysis pubis.

Marshall and his colleagues (1949) have devised another operation which is widely used in U.S.A. and England.

If a patient has stress incontinence and a cystocele, the operation should be an anterior colporrhaphy. If, however, there is no cystocele, either an anterior colporrhaphy or an Everard Williams operation can be done.

(B) STRESS INCONTINENCE DUE TO CONGENITAL WEAKNESS OF THE INTERNAL SPHINCTER OF THE BLADDER :

The degree of incontinence in this type varies considerably. In extreme cases it is almost complete as the internal sphincter is grossly defective in structure. In less severe cases the patient will lose control only occasionally and only during a hearty laugh or cough. In severe cases, the girl is brought for medical attention at an early age, as the incontinence is disabling; but in the less severe cases, the patient usually comes as an adolescent or young adult, because the occasional stress incontinence has become an embarrassment only when the young girl becomes more seriously conscious.

In all cases of weakness of the internal sphincter there will be an associated frequency and urgency of micturition which may become sufficiently troublesome to make the patient seek medical advice. Sometimes a mild degree of congenital weakness of the sphincter will suffer from nocturnal enuresis.

By cystometric measurements, severe cases have revealed an absence of part of the internal sphincter; while in other cases, the internal sphincter appears to be more widely open than normal and to be funnel-shaped.

In severe cases, surgery should be advised and carried out in early childhood. In less severe cases, surgery should be delayed until early adult life—for, there is often improvement in the incontinence as the patient grows up. Surgery should never be advocated for just an occasional leak of urine when the girl laughs or giggles.

It is surgically impossible to make an effective muscle sphincter. The best that can be done is to close the patulous internal sphincter until the opening from the bladder into the urethra is very small indeed and thereby create some resistance at the internal sphincter to the escape of urine. When the formation of the internal sphincter is grossly defective this operation of tightening the internal sphincter through the open bladder will benefit the patient; but in less severe cases success is not sufficiently certain to warrant operation. Each case should, therefore, be considered individually and operation only advised if the incontinence is having a serious effect on the well-being of the patient.

If incontinence persists after such an operation there is no alternative but to consider deviation of the urine either by transplantation of the ureters into the colon, or by bringing the urethra forward to open on the abdominal wall. There is no satisfactory bag or appliance for incontinence in the female.

(C) STRESS INCONTINENCE DUE TO DAMAGE OF THE SPHINCTER OF THE BLADDER :

Damage to the sphincter may sometimes be due to a gynaecological operation. A profound disturbance indicates that the bladder sphincter has become almost completely damaged. The symptoms are marked frequency of micturition both by day and by night and incontinence of the urgency and stress type.

The internal sphincter is not only a single circular bundle of muscle fibres surrounding the neck of the bladder, but in addition sphincter fibres pass from the bladder neck down the urethra in encircling loops. The urethral fibres appear to be important and probably are able to maintain continence if the bladder neck bundle is completely damaged. Both segments of the internal sphincter are exposed to injury in a total hysterectomy or anterior vaginal operation. But even if one segment of the internal sphincter is damaged the remaining fibres are usually able to maintain continence. Where injury to the sphincteric fibres has been very great or else the undamaged segment is unable by itself to maintain continence that disturbance of micturition occurs. In these cases there will not be any bladder neck descent and no operation will be of any avail. Treatment of these cases is very uncertain, but tightening of the internal sphincter through the open bladder should be tried if the symptoms are severe. If this procedure fails, deviation of the urine will be inevitable.

—From an article by Harland Rees, *Med. Press*, **246**: 293, 1961.

CURRENT MEDICAL LITERATURE

Phenformin in Oral Therapy in Diabetes

BLOOM, A. AND RICHARDS, J. G. (*Brit. M. J.*, **1** : 1796, 1961) from Whittington Hospital, London, write :

Chlorpropamide is both effective and well tolerated by most diabetics who fail to respond to dietary restriction but who do not become ketotic. Whether these patients are newly diagnosed or whether they have been controlled previously on a small dose of insulin, normoglycaemia can usually be maintained by a dose of 500 mg. a day, later reduced to 350 mg. or less. Nevertheless, many diabetics expected to respond to this tablet therapy in practice fail to do so. Others who respond initially to chlorpropamide begin to relapse after a time despite continued adherence to a diet. It is in such cases that phenformin offers the opportunity of prolonging oral therapy without recourse to insulin.

Phenformin is a powerful hypoglycaemic agent, but it so often gives rise to gastro-intestinal intolerance when administered in the maximum therapeutic dose that it is not as suitable as the sulphonylureas for general use. However, when given at a dose of 100 mg. a day it is reasonably well tolerated by most, and can be administered conveniently in the form of a single slow-disintegration capsule. Although this is a comparatively small dose of phenformin, it effectively controlled hyperglycaemia in some diabetics in whom chlorpropamide was inadequate. In a greater number of diabetics in whom chlorpropamide was unsatisfactory, however, substitution by phenformin was ineffective, but control was obtained when the two agents were administered together. Hence it would seem convenient in patients responding poorly to chlorpropamide to try the addition of phenformin before recourse to insulin.

Diabetes is a progressive disease, though the rate of progression varies greatly. It is not surprising that some patients at first controlled by the sulphonylureas slowly began to relapse, and this was equally true of patients controlled on combined therapy. In some patients the introduction of combined therapy has meant no more than a delay before insulin was introduced. Nevertheless in other patients treatment by combined therapy has been prolonged, and has been particularly welcomed by elderly patients who would otherwise have required insulin.

Whereas it seems clear that oral therapy as at present described is capable of maintaining normoglycaemia, it remains open to question whether this is sufficient to prevent the degenerative complications so commonly seen in diabetics poorly controlled on insulin, since these complications could possibly be due to factors other than hyperglycaemia. However, quite apart from ultimate complications, hyperglycaemia leads to troublesome symptoms and predisposes to infection. In the present state of our knowledge, these seem valid reasons to justify the use of oral therapy in responsive patients.

Of 1,450 diabetic patients attending a clinic, 587 (40·4 per cent) were controlled on simple dietary restriction, 608 (42 per cent) required insulin, and the remaining 255 (17·6 per cent) took oral hypoglycaemic agents.

Diabetics seemed suitable for oral therapy who failed to respond to chlorpropamide, were given phenformin in small doses as an alternative or as adjuvant therapy. Of 23 such patients, 9 responded to phenformin alone but 14 responded only when the phenformin and chlorpropamide were given together.

Phenformin when administered in a single daily 100 mg. slow-disintegration capsule appeared to offer as effective clinical control as when given in divided doses as tablets.

Guanethidine in the Treatment of Hypertension

BAUER, G. E., CROLL, F. J. T., GOLDRICK, R. B., JEREMY, D., RAFTOS, J., WHYTE, H. M. AND YOUNG, A. A. (*Brit. M. J.*, **2** : 410, 1961) from the cardiovascular clinic, Sydney Hospital, write :

Guanethidine sulphate, a new potent oral hypotensive agent, was administered to 28 patients for a period of up to 12 months. This drug selectively blocks adrenergic nerve transmission, leading to sympathetic inhibition with marked postural fall in blood-pressure without any parasympathetic blocking effect such as blurred vision, dryness of mouth, constipation, and bladder atony. Its prolonged action makes it suitable for long-term outpatient treatment provided certain precautions are taken. It is best given in conjunction with saluretic agents such as chlorothiazide or hydrochlorothiazide. Drug tolerance has not been a problem, and side-effects have been slight except for the appearance of depressive symptoms in four patients. Guanethidine has been compared with another adrenergic blocking agent and has been found to be a more suitable drug for routine clinical use.

Chronic Pyelonephritis

KIMMELSTIEL, P., KIM, O. J., BERES, J. A. AND WELLMANN, K. (*Am. J. Med.*, **30** : 589, 1961) from the departments of pathology and medicine, Milwaukee County Hospital, and Marquette University School of Medicine, Milwaukee, Wisconsin, write :

The reliability of morphologic criteria for the identification of chronic pyelonephritis and its sequelae is more limited than generally conceded. The authors have attempted to outline criteria which can be employed more reliably for this purpose, and find that, using such more rigid criteria, the prevalence of chronic pyelonephritis does not vary significantly from decade to decade, with the possible exception of childhood. It also appears that the clinical significance of this disorder in respect to renal function is less than most recent statistics seem to indicate.

Caution must be exercised in distinguishing the sequelae of primary vascular lesions and developmental abnormalities from changes due to pyelonephritis. Certain guides to that end are offered.

The reliability of estimates of the frequency with which unilateral chronic pyelonephritis causes hypertension is open to question. The significance of bacteriuria and its relation to pyelonephritis is yet to be evaluated more completely. Bacteriuria cannot at present be identified with "inapparent" pyelonephritis. One has yet to learn why in a limited number of patients with acute pyelonephritis the disease progresses into a chronic non-

obstructive phase, and whether indeed this insidious process is a continuation of pyelonephritis, as originally defined, or whether it is of an altogether different nature.

Primary Aldosteronism

BIGLIERA, R. G. AND FORSHAM, P. H. (*Am. J. Med.*, **30**: 564, 1961) from the metabolic unit, University of California School of Medicine, San Francisco, California, summarise their findings as follows: Two patients with primary aldosteronism, accompanied by hypertension, hypernatraemic, hypokalaemic alkalosis and severe potassium depletion, were demonstrated to have an increased volume of extracellular fluid. A marked rise in plasma volume without any change in red cell volume was observed. Changes in sodium intake failed to alter the expanded state. Only minimal responses to salt-retaining hormones were present. Rapid infusion of isotonic saline solution produced a rapid rise in the filtered load, with rapid excretion of sodium and maintenance of the *status quo* in aldosterone secretion. The rapid changes in glomerular filtration rate appear to be a factor in limiting further increases of this chronically expanded state and would explain, in part at least, the lack of oedema observed in these patients. In contrast, the tumours were shown to respond to changes in plasma volume, corticotropin, SU-4885 and spirolactone, thus demonstrating their physiologic responsiveness to uncompensated stimuli. Growth hormone was shown to have a sodium-retaining action independent of aldosterone secretion.

Erythrocyte Sedimentation Rate: Mechanism and Significance

RUHENSTROTH-BAUER, G. (*Brit. M. J.*, **1**: 1804, 1961) from Manx Planck Institute for Biochemistry, Munich, writes:

A high sedimentation rate is caused by specific plasma proteins which are designated agglomerins. They resemble incomplete antibodies in that they require for their expression a high-molecular non-specific supplement. Every plasma contains a pro-inhibitor of sedimentation which is activated at body temperature by means of a specific lipase. A glucolipid fraction can be obtained from erythrocytes that contain the substance which combines with the agglomerins. A concentrate of this receptor substance added to whole blood (50 μg./ml.) decreased the sedimentation rate by 50 per cent. A fraction from *E. coli* will on administration to rabbits produce a high sedimentation rate. Rabbits, like man, then produce agglomerins, of which fibrinogen is only a minor part. Almost all anti-inflammatory substances are inhibitors of agglomerin action. It is suggested that agglomerins are involved in the inflammatory response and that their action on the red cells is only coincidental.

Purulent Meningitis in Childhood

KNEEBONE, G. M. (*M. J. Australia*, **2**: 124, 1961) from the department of child health, University of Adelaide, writes:

Two hundred and thirty-seven cases of purulent meningitis were treated in the Adelaide Children's Hospital over a seven-year period and have been reviewed. Forty-one patients died (17·3 per cent) and there is no indication of an appreciable improvement in mortality rates during this period.

The age incidence has been discussed in relation to the transfer of maternal antibodies, and the seasonal incidence has been recorded.

It is advocated that treatment should be limited to those drugs which act specifically against the type of meningitis under consideration. It is further suggested that varied combinations of multiple antibiotics have contributed to the poor results obtained in the past, both in regard to the mortality and to the incidence of complications and sequelae.

The 'unknown' group of cases has been discussed, and the nature of the meningitis, in relation to therapy and prognosis, interpreted as representing a less severe form than the diagnosed types of meningitis.

Neonatal meningitis has been considered to present the problems of delayed diagnosis and of overwhelming infection at this age. Chloramphenicol is suggested to be the best single agent in meningitis in the neonatal age group.

The non-specific character of the clinical picture is reiterated and the significance of rashes, respiratory symptoms and cyanosis discussed.

The contention is put forward that the fundamental problem in childhood meningitis is delayed diagnosis, arising from unawareness of the possibility of this condition being present. Childhood meningitis still presents a serious problem to those who treat children.

Amoebic Panorama

ACEVEDO, A. O. (*Dis. Colon & Rectum*, **4**: 235, 1961) from Mexico City writes:

To provide an idea, as accurately as possible, of amoebiasis in Mexico, a review was made of the reports of 218 writers, the majority of them being Mexican. This study covered data recorded from the period prior to the Conquest (1519) to the present day. The author compiled a list of 88,998 examinations which have been carried out in Mexico and they showed an average of 23·9 per cent of amoebic persons. The multiple sequelae and complications caused by amoebiasis are described in this paper and even amoebiasis of the uterine cervix, which is extremely rare, is described.

Six thousand seventy-one case histories were studied, of which 1,200 were of amoebic patients who belonged in the following categories:—carriers, 34·7 per cent; monosymptomatics, 18 per cent; alternate syndrome, 16 per cent; chronic intestinal stationary syndrome, 12·6 per cent; flatulence syndrome, 13·8 per cent; hyperaesthenic syndrome, 11·7 per cent; diarrhoeic syndrome, 8·6 per cent; dysenteric syndrome, 5 per cent; cephalalgia syndrome, 2 per cent; Konig's syndrome of 'tumoral nature', 4 per cent; stenotic syndrome, 30 per cent, and gastroduodenal ulceration syndrome, 0·075 per cent. All syndromes described above are associated and alternate amongst themselves and very seldom are they single entities in their original state.

From the records of thoracic patients of the General Hospital of Mexico City, 135,610 x-ray plates were

examined, which revealed 1,298 (0·99 per cent) hepatic abscesses. What we call 'abscessoscopy', a procedure that reveals the multiplicity of forms of abscesses, was studied. In this paper the author describes, also, the first occasion on which man was able to look into the interior of the cavity of a hepatic abscess in a living person. The study of the permeability of the hepatic abscess wall is succinctly reported.

A separate group of 100 patients, all of them amoebic, were studied. After having treated them with chlorophenoxamide, it was learned that two patients did not tolerate the treatment and in 95 of the remaining 98, of whom six received a double treatment, a parasitologic cure was achieved.

Cytological Studies in Early Detection of Cancer

CRABBE, J. G. S. AND EGERTON, M. E. (*Brit. M. J.*, 1 : 1790, 1961) from the department of pathology, Royal Free Hospital, London, write :

In the comparatively few centres in this country where the cytological diagnosis of cancer has been practised for some years the successes have been such that the demand for its use has tended to increase. This is exemplified at the Royal Free Hospital where during a brief period of some six years the successes of one or two research workers have resulted in the establishment of a department devoted exclusively to cytological cancer diagnosis with facilities for both teaching and research work. During this time the great advantages of the technique have become apparent.

Firstly, and most important, as a routine procedure it can be used to detect tumours at a very early stage of development, often before signs and symptoms appear. It is simple to perform and need cause no alarm, inconvenience, or discomfort to the patient, and thus it can be repeated as often as may be necessary. The only inconvenience that a patient may be caused is in obtaining those materials where needles or other instruments have been used.

The chief disadvantages of the method are the time that is required to read the slides and the lack of trained personnel to do this. The taking and processing of the smears is simple, but the interpretation of the wide range of the cellular variations in the different types of body fluids requires considerable training. Until recently it was usually found necessary to go to America to gain the requisite experience, but now one or two cytological centres in London and the provinces provide facilities for teaching the technique and the interpretation of the smears. This should help to eliminate the necessity for sending personnel abroad for training, with the concomitant expense which that involves.

A plea is made for the more extended use of the method throughout the British Isles, where much of the original pioneer cytological work was done. The experience of cytological workers all over the world shows that the technique is well worth while, for if the detection of cancer when it is symptomless and at a very early stage of development is going to save or prolong lives—and there is reason to believe that it does—then the method is a most valuable weapon in the fight against cancer.

NOTES AND NEWS

Control of Soil-transmitted Helminths

Among all the species of worms parasitic in man the soil-transmitted intestinal nematodes—the roundworm, the whipworm, and the hookworm—hold the distinction of exerting the greatest influence on individual health and group productivity throughout the world, their prevalence in different communities serving indeed as an index of social and economic standing. Although they cause anaemia, reduce physical and mental capacity, weaken resistance to other diseases, and at times affect health directly and severely, attempts at their control have met with disappointing results. As a consequence they present a health problem that is apt to be given perfunctory attention or even neglected. Prof. Beaver discusses the factors involved in the control of these soil-transmitted helminths, the control methods that have been used and should be used, and the research which problems of control raise (Control of Soil-transmitted Helminths—Paul C. Beaver, W. H. O., Public Health Papers, No. 10, 1961, Pp. 44, Price 3s. 6d.) A section is devoted to other miscellaneous helminths the role of which in parasitic infections is still somewhat obscure. An annex deals with diagnostic methods. (*Nature*, September 23, 1961).

Germ-Free Diet for Patients

British pioneering work on prepacked special diets made germ-free by irradiation could lead to the setting up of a service for supplying smaller hospitals overseas, reports BIS. Requirements could be met for the special sterile diet needed for some patients following certain operations.

The possibility arises from work done by doctors and dieticians at London's Hammersmith Hospital in collaboration with scientists at the British Atomic Energy Authority's radiation laboratory at Wantage, Berkshire. Germ-free diets are needed for patients who lose their resistance to disease after being treatd with massive doses of radiation given, for example, when it is necessary to try to replace a defective kidney with a sound one. After the operation, the patient has to be nursed in germ-free conditions and even given sterile food.

Dieticians and bacteriologists at Hammersmith Hospital found that satisfactory results could be obtained by sterilising prepacked deep-frozen food with gamma rays using special equipment at the Wantage laboratory.

The irradiation plant at Wantage uses cobalt-60 sources of gamma rays made at Calder Hall, Cumberland. Similar equipment is now being marketed by Vickers-Armstrongs for the sterilisation by batch or continuous flow of disposable medical equipment like bandages, surgical gloves or hypodermics; of hair or wool for industry; and of grain to remove weevils and similar pests.

Teaching Psychiatry and Mental Health

The need for reform of the medical curriculum in training doctors has been the subject of much contro-

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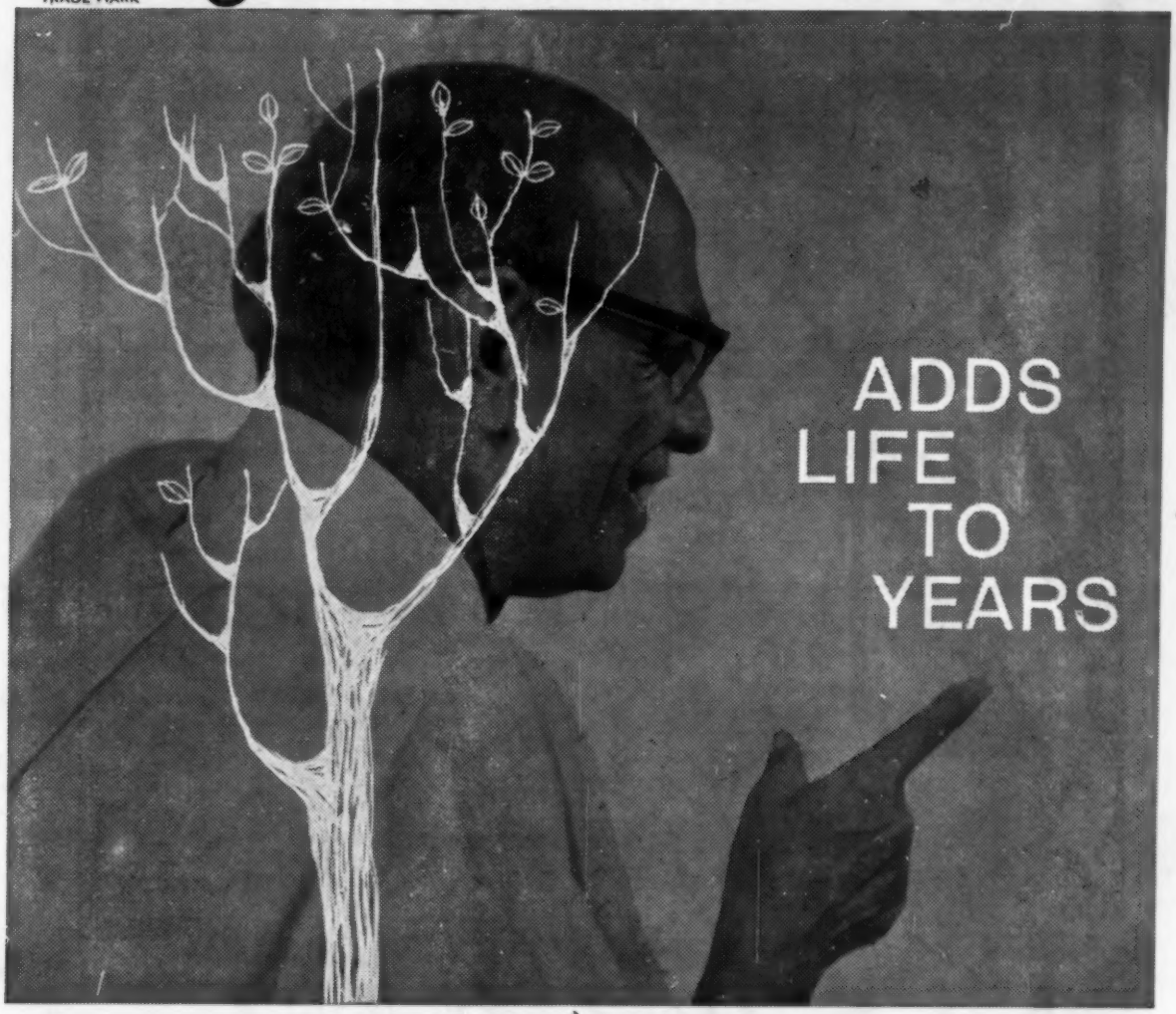

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versy, and the place that psychiatry should occupy in the curriculum has often been at the centre of the controversy. The reason for this is twofold. Psychiatry as a medical speciality has now developed to the stage at which it can claim a place of its own in the company of other branches of medicine; it is considered by many to be a leaven permeating medicine as a whole and re-orientating medical practice and medical teaching from its present tendency to separate into compartments towards a better awareness of the human being. A publication (Teaching of Psychiatry and Mental Health, World Health Organisation) brings together a group of papers by teachers of psychiatry from various parts of the world, describing how the teaching of psychiatry and mental health care can be organised, what problems of content and method are likely to arise, and in what way the teaching should be integrated into the medical curriculum. The authors demonstrate the relationship of psychiatry and mental health to clinical medicine and the sciences of man. They examine the role of neurological investigations in the teaching of psychiatry, the teaching of medical psychology, and the social character of mental disorder. There is also a description of how psychiatry is taught at present in different countries and of the principles being adopted in guiding its future development. The publication presents the basic argument in favour of more psychiatry in the medical curriculum and shows how this can be achieved. (*Nature*, September 23, 1961).

Unidentified Substance Controls Spread of Cancer

An unidentified substance in the pituitary gland which apparently controls the growth and spread of body-invading cancers has been reported by Dr. Bernard Fisher and Dr. Edwin Fisher. Their experiments with rats indicate that the substance possibly hormones from the gland, regulates in some way the journey of cancer through the blood stream to distant organs, particularly the liver. They found that when the pituitary was removed the spread of cancer was considerably reduced. (*Scientific Bull.*, USIS, July 26, 1961).

Blood Stains Reveal Sex

Although most proposals for determining sex by either microscopic or chemical means have remained theoretical, a workable method of determining a person's sex from bloodstains has been recently described, reports *Science Digest*.

This system, as outlined by Professor T. Oki of Kagoshima University before a meeting of the Society of Medical Jurisprudence of Japan, can use bloodstains up to four months old. The stains are dissolved in a 0·53 per cent solution of acetic acid. They are then fixed, dyed, and examined microscopically.

This process reveals the neutral multinuclear leucocytes. In females, these nuclei abound in unusual configurations called "drumsticks." There are knobs attached to the body of the nucleus by a single filament. The number of drumsticks in the sample gives a clue to the sex of its owner.

A qualification as to the size of the drumsticks was made by Dr. Ursula Mittwoch, of University College, London, who says the singularly appended knob must have an exact diameter of 0·0015 mm. There are other similar structures, she says, which appear in the blood but are valueless in sex determination.

Dr. Mittwoch, in a recent contribution to the *New Scientist*, describes in detail how it is now possible to tell whether a drop of blood has come from a man or a woman.

Rehabilitating Lepers

Of an estimated world total of 10 million people suffering from leprosy, probably not more than 20 per cent are receiving treatment of any kind for the severe disabilities that the disease often causes. The World Health Organisation scientific meeting on rehabilitation in leprosy, through an on-the-spot examination of leprosy patients with typical varieties of deformity at a research sanatorium in India, set out to determine the extent of the problem of disability, to advise on the best application of available knowledge in prevention, treatment, and rehabilitation of disabled leprosy patients, and to recommend further research. (*Nature*, September 23, 1961).

New Data on Pathogenesis and Treatment of Oedema

Dr. Boudnik, head of the Soviet Pediatric Centre attached to the Kalawati Saran Children's Hospital, advanced new data on oedema in a lecture he delivered at Travancore House before a select audience of doctors and medical students. The results of recent researches in the mineral metabolism of the organism on the one hand and the physiological functions of the system governing the function of the kidneys on the other, he said, have made it possible to reconsider previous conceptions of the origin of oedema and to work out basically new lines of treatment. According to the modern view, he added, whatever the cause of oedema—certain disorders of the heart or liver or lack of protein, etc.—it develops as a result of damage to the delicate mechanisms which regulate sodium and fluid excretion from the body. He explained in some detail the working of these mechanisms and how disturbance in them leads to the retention of fluid in the body. Speaking about the treatment of oedema, Dr. Boudnik said that the first thing was not the administration of diuretic drugs, but action on the primary or leading link of a pathologic chain. He mentioned in this connection certain compounds of steroid structure known under the collective name, spirolactones, which have been synthesised recently and which tend to prevent the retention of sodium in the body. These compounds, he suggested, are of inestimable value in the treatment of oedema As for diuretic drugs, Dr. Boudnik said, organic compounds of mercury had held the field for more than three decades, despite the fact that they often caused toxic and allergic reactions. In recent years, however, they had been superseded by new sulphonamide diuretics such as chlorothiazide and its derivatives. Although the mechanism of the diuretic action of chlorothiazide

was still unknown, Dr. Boudnik said, it was almost as effective as mercury diuretics though far less toxic, and was of great value in the treatment of oedema. He explained in detail the action of chlorothiazide and various derivatives of chlorothiazide on oedema, the dosages in which they might be given and the precautions that have to be taken. He cautioned in particular about giving chlorothiazide to patients with cirrhosis of the liver as this might result in a coma. Questions were asked after the lecture was over, and later a couple of documentaries on Soviet medicine were shown. (*News & Views from Soviet Union*).

The Alvarenga Prize for 1961

On July 14, 1961, the College of Physicians of Philadelphia awarded the Alvarenga Prize for 1961 to Dr. Seymour S. Kety, M.D., Professor of Psychiatry, Johns Hopkins University, for his outstanding work on cerebral blood flow and the effect of drugs on the central nervous system.

The Alvarenga Prize was established by the Will of Pedro Francisco DaCosta Alvarenga, of Lisbon, Portugal, an Associate Fellow of the College of Physicians of Philadelphia, to be awarded annually by the College of Physicians on the anniversary of the death of the Testator, July 14, 1883.

Trans-International Psychosomatic Seminars

The Trans-International Psychosomatic Seminars of New York will go out on a trip around the world in the winter of 1962-63. Each teaching seminar will consist of lectures discussing the interrelationship of the psyche and the soma and the need for the understanding of psychosomatic medicine in the practice of medicine and surgery. Moving picture films and slides, depicting the use of psychosomatic techniques will also be used. The seminar will visit Bombay on 4-6/12/1962.

The seminar took a trip around the world first in the winter of 1954-55 and next in the summer of 1957. Because of the acceptance of these educational services, this third trip has been organised.

Human Embryo Kept Alive

Soviet scientists have been able in some experiments to keep an artificially cultivated human embryo alive until it weighed up to 500 g. (about 17½ oz.), a Russian medical scientist said on a Moscow television programme.

Professor Pyotr Anokhin said that studies on human embryos have been conducted in Russia for 15 years. He was appearing on the programme with the Italian scientist, Professor Petrucci, who described his own experiments on the cultivation of a human embryo in a test tube.

Viewers saw excerpts from films recording various moments of the development of the embryo and the equipment used by the Italian.

Italian newspapers reported last January that Professor Petrucci and two assistants fertilised a female ovum with male semen and kept the resultant embryo alive for 29 days.

Growth Halted and Life Doubled

American biochemists have doubled the life of mice and chicks by halting their growth with a change of diet.

Dr. Caroll Hochwalt made this statement recently at the inauguration of a research centre for Monsanto chemical products at St. Louis (Missouri). He said the change of diet consisted in eliminating the amino acids which enable the body to create proteins essential to growth. Dr. Hochwalt said similar experiments had been made on chicks during periods of six to nine months. He would not say whether similar techniques could succeed with humans.

Spinach and Tea leaves to Resist Atomic Fallout

The Surgeon-General of the KMT Defence Ministry has advised people of Formosa to eat more spinach and tea leaves to help resist atomic fallout on his claim that spinach and tea leaves (preferably black tea leaves) contain oxalic acid which can absorb radioactive substance in the human body.

According to a Hague report thousands of radiactive geese, ducks and other migratory wild fowl are currently filying from the direction of Scandinavia towards the Netherlands bringing with them a potentially serious public health hazard.

Government circles, it is stated, considered the danger so great that they had organised an intensive enquiry into the degree to which the birds have been contaminated by radioactive material. All wild geese killed in the Netherlands were to be checked for radioactivity and the results of the enquiry would decide the public health measures to be taken.

Nearly 500 Million Live in Starvation

Between 300 and 500 million people are starving owing to lack of food, the Indian Director General of the Food and Agricultural Organisation of the United Nations, Dr. B. R. Sen, told a press conference at Hague on 28-10-61.

The Director General of the F.A.O. arrived in the Netherlands on the occasion of an anti-famine campaign which will start in the Netherlands under the auspices of "Novib", Netherlands organisation for international assistance, and the F.A.O. Committee, UNESCO Centre and UNICEF Committee of Netherlands.

Gift of Polio Vaccine from Soviet Red Cross

Officials of the Soviet Embassy called on the Director-General of Health Services, Lt.-Col. V. Srinivasan, and delivered 20,000 doses of vaccine for the treatment of poliomyelitis in Delhi as a gift from the Soviet Red Cross. Mr. Srinivasan expressed deep gratitude to the Soviet Union for the gift.

In the spring and summer this year there was an outbreak of poliomyelitis in Delhi. The authorities of the Delhi Medical College, Lady Hardinge Hospital and Kalavati Saran Children's Hospital had requested the Soviet Red Cross to assist them in eliminating the disease. The vaccination of children will start soon.

Immunisation against Polio

Nearly 20,000 children below the age of five are expected to be covered by a Delhi Corporation scheme of immunisation against poliomyelitis.

A Corporation spokesman said on 30-9-61 that the programme was being organised in collaboration with the department of preventive and social medicine, Lady Hardinge Medical College and the Kalavati Saran Children's Hospital.

The Corporation has chosen Paharganj, with an estimated population of one lakh, for introducing the scheme.

A house-to-house campaign will be undertaken by 70 students, in teams of two, drawn from the Lady Hardinge Medical College, College of Nursing and the Lady Reading Health School. The immunisation work is expected to take a fortnight.

Twenty thousand capsules of oral vaccine have been obtained from the Red Cross and the Red Crescent Society of the U.S.S.R.

Mobile Clinic-Gift by IPPF

A Mobile Field Clinic and Education Unit for family planning work to be run by the Family Planning Association of India in a Block Development area in Maharashtra which cost Rs. 55,000, was received by the Association as a gift from the International Planned Parenthood Federation.

Mrs. Dhanwanthi Rama Rau, President of the Association, said that the gift unit, financed through contributions from American friends, including a substantial amount from the Aaron E. Norman Fund, was presented by Mr. Hugh Moore, the founder and steering committee chairman of the World Population Emergency Campaign, to Mrs. Moeena Roy, wife of the Indian Consul-General in New York, before it was shiped to Bombay.

She stated that this would be the first unit to be run by the Association and would serve as a pilot project in introducing mobile family planning education and clinical services in the rural areas, which would otherwise not receive such help.

The Association would staff the unit with a doctor, a health visitor and a social worker and would be responsible for directing and financing it. The project was estimated to cost Rs. 20,000 to Rs. 25,000 annually, she added.

Health and Disease in Ancient Harappa

Four thousand and 500 years ago people in India suffered from anterior poliomyelitis, pyorrhoea, rickets and bone tuberculosis. Their life expectancy was about 40 years.

These and other data have been revealed from the recent palaeo-pathological study of the 260 human skeletal remains found in Harappa (Montgomery district, now in West Pakistan) between 1922 and 1946. The Indus civilisation specimens date back to earlier than 2,500 B.C. and the culture covers about 1,000 years.

Such a study of diseases through examination of prehistoric skeletal remains has been undertaken for the first time in India under the auspices of the Anthropological Survey. The specimens are now under examination at the Survey Office in the Indian Museum, Calcutta.

No evidence of calcination is gathered from the remains, nor is there any sign of the art of embalming bodies.

Signs of deformation of long bones, inflammatory condition of bones, gigantism and dwarfism are evident. The worn out condition of cusps of the teeth of the skulls examined suggest the coarse food habits of that time.

Minister Inaugurates TB Home Treatment Scheme

Union Health Minister D. P. Karmarkar inaugurated the 12th T.B. Seals campaign by purchasing a seal book from a nurse at a public function at Delhi on October 2, 1961. The campaign will end on January 26 next.

The Minister also initiated the Corporation's home treatment scheme for Tuberculous patients. Costing Rs. 2 lakhs, the scheme will initially cover some of Delhi's worst congested and insanitary areas where nearly 3,500 Tuberculous patients live.

Mr. Karmarkar expressed his distress that the T.B. seals sale campaign was gradually losing popularity. The sales had gone down from nearly Rs. 12 lakhs in the first campaign to about Rs. 5 lakhs last year. He appealed to Ministers and public leaders to go from door to door for raising funds to fight T.B. Unfortunately, he said, the pride and prestige which public men used to feel in begging for a public cause had now disappeared.

Taking into account the shortage of beds in hospitals, the incidence of the disease and the mortality rate, Mr. Karmarkar said that the most effective way to combat the disease was through home treatment.

Red Cross Clinics, Medical Units & T.B. Hospital

The West Bengal Government will undertake the responsibility of maintaining all maternity clinics, medical units and also a tuberculosis hospital now run by the Red Cross at different places in the State. This will involve an expenditure of about Rs. 2 lakhs annually.

An announcement to this effect was made by Chief Minister Dr. Roy inaugurating the "Red Cross Month" in the State at a function held at the Raj Bhavan lawn on 7-10-61 in the presence of a distinguished gathering.

But the financial responsibility of maintaining 22 free beds in K. S. Ray T.B. Hospital, Jadavpur, involving about Rs. 54,000 annually would remain with the Red Cross as now.

Dr. Roy also announced that the State Government might henceforth request the Red Cross to carry on relief work in emergencies such as fire havoc, flood devastation and riots. The State Government, he said, would bear the financial respoisibility in such matters.

T. B. Studies at Bangalore

Under the national tuberculosis control programme, undertaken by the Government of India with the assistance of the World Health Organisation and United

Nations Children's Emergency Fund, studies have been made on community and individual awareness of tuberculosis, on causes of failure to take treatment, on drug acceptability and on the economic effects of T.B.

The National Tuberculosis Institute at Bangalore has also initiated a rural and urban control programme under which victims are located and put under treatments.

Re-testing of BCG-vaccinated people has been completed in four States. A study of tuberculin allergy among vaccinated and non-vaccinated school children has also been made.

Hygiene Exhibition Opened

A hygiene exhibition organised by the German Hygiene Museum, Dresden, and the Society for Cultural Relations with Foreign Countries of the German Democratic Republic, was opened at the Muslim Institute Hall, Calcutta, on 3-10-61. Dr. H. K. Roy, president, West Bengal Branch of the Indian Medical Association, inaugurated the exhibition.

The exhibition explains the essentials of health and hygiene and the human anatomy and the functions of the principal organs, through charts, diagrams and models in a way that makes knowing a pleasure. The body of a human female done in glass with the skeleton and nervous system seen through the glass-flesh is a striking exhibit. The models are precise and life-like. Even a layman comes out of the exhibition with some useful knowledge of diseases and prevention imparted through a delightful audio-visual medium.

It was fun as well as a medical check-up measuring one's vitality through a gadget. Enthusiasts who had their vitality measured were disappointed to find them invariably falling below the normal.

3-Year Plan to Root out Smallpox in U.P.

A three-year scheme to eradicate smallpox from Uttar Pradesh will be launched on April 1, 1962. Part of an all-India scheme, the project aims at mass vaccination of the whole population at a cost of Rs. 1·2 crores.

Fourteen districts will be taken up in the first year. The Epidemic Diseases Act will be invoked in all these districts to make vaccination obligatory on everyone.

India, Burma and Pakistan are the only countries where smallpox remains a public health problem of considerable magnitude. U.P. is the worst State in mortality and morbidity. It is estimated that more than 16 lakh persons have died of smallpox in the State in the last 80 years. The worst year was 1951 when 49,000 persons died of it.

The districts where the scheme would be enforced next year are: Almora, Naini Tal, Pithoragarh, Bareilly, Budaun, Moradabad, Rampur, Faizabad, Pratapgarh, Philibhit, Gonda, Bahraich, Bara Banki and Bijnor.

Alcoholism is a 'Major Problem'

Maj. (Mrs.) Karamjit Kochar of the Army Medical Corps said at New Delhi on 21-9-61 that the incidence of tuberculosis among alcoholics was ten times higher than among others.

She was speaking on "Intoxicants and Narcotics" at a meeting of the Delhi Rotary Club in New Delhi.

Dr. Kochar said there was not a single organ of the human body which did not suffer from the after-affects of intoxicants.

Alcoholism was considered to be the world's fourth major public health problem, Dr. Kochar said. The use of intoxicants was sapping the vitality and energy of the working classes. Something had to be done to keep them away from this addiction, she pleaded.

Training for Drug Technologists

Two hundred and seventy technologists, engineers and chemists will be deputed for training in Russia before the end of next year to man the four drug factories of the State-owned Indian Pharmaceutical and Drug Company.

The trainees will include mechanical engineers, and those who have specialised in technology and chemistry, with an adequate background. After training, they will take over from about 252 Russian engineers who will be in India installing the four factories of antibiotics at Rishikesh, synthetic drugs at Hyderabad, phyto-chemicals at Neriamangalam in Kerala and surgical instruments at Guindy, Madras. The fifth factory, that of hormone and glandular products to be started in Bombay has been deferred for lack of a modern slaughter-house. The training period will range from six months to one year.

The synthetic drug factory will have 100 Russian engineers to work, while the number to be sent to Russia for training for this project will be 127, the largest contingent for the four factories. The number of trainees may be increased.

Leprosy Programme Advisory Body

The Government of India has appointed a high powered Committee to advise the Government on leprosy programmes with the Union Health Minister, Dr. D. P. Karmarkar, as Chairman and Dr. Y. K. Subramanium, Assistant Director-General of Health Services, as secretary.

At the 11th meeting of the Governing Body of the Central Leprosy Teaching and Research Institute held at Hardwar on October 22, 1961, Mr. D. P. Karmarkar who presided said that they should go away from big cities to distant towns to strengthen the programme of fighting leprosy.

The Institute is being run by the Union Government in collaboration with the Madras Government for conducting research, training and treatment in leprosy.

New Operative Procedures for Treatment of Leprosy

New operative procedures for treatment of leprosy have been evolved at the Vellore medical hospital to restore normal functioning of parts afflicted by the disease.

Count Raoul Follerean, president of the Order of Charity, Paris, who revealed at a new conference on October 28, 1961, said 40 doctors representing 20 coun-

tries had come to the Vellore hospital to study these procedures.

Count Raoul said the medical world was of the unanimous opinion that leprosy was a perfectly curable disease and that it was much less contagious than tuberculosis. The important factor in the cure of leprosy, according to him, was the removal of the fear complex from the minds of the patients which in itself would pave the way for early eradication of the disease.

Count Raoul, who was on a 12-day tour of the State, visited a number of leprosy institutions and left for Delhi on way to France.

Lunatic Women and their Cure

The West Bengal Government is understood to have authorised a voluntary organisation to undertake psychotherapy of lunatic women in jails.

The relevant scheme has been initiated by the YWCA. With the help of students of experimental psychology, this women's organisation will undertake a study of lunatic women in jails to ascertain the number of cases which can be taken up for psychotherapy.

The jail population of lunatic women,—216 at present, including criminals, has posed a problem to the Government for various reasons. One important point in this connection is that once a lunatic woman is admitted to a jail, she becomes completely separated from her family.

In most cases, it is stated, these women, even though they have chances of recovery after treatment, are not taken back into families from which they come. As a result, the Government has to take charge of these women almost on a permanent basis. The difficulty with them is that quite often these women are involved in cases of assaults and rowdism.

The Government has, therefore, asked the women's organisation to ascertain the number of cases, which can be reasonably expected to return to normal life after prolonged treatment. It is with this object in view that the YWCA will undertake the scheme on voluntary basis.

Stress on Balanced Diet

The need for introducing a balanced diet for building up a healthy and strong nation was stressed by Dr. B. C. Roy, Chief Minister of West Bengal on 12-10-61.

Dr. Roy was inaugurating the Mobile Nutrition Extension Scheme of the West Bengal Government at Harinabhi within Sonarpur police station in 24-Parganas district about 16 miles from Calcutta. On this occasion a Mobile Demonstration Unit for preparation particularly of popular wheat products was received from the Wheat Associates of America.

Dr. Roy in his speech referred to the present scarcity and high prices of meat and fish and said protein contents of food could be largely substituted if people took wheat products as one of their two meals in a day. The unit that he inaugurated would not only popularise the use of wheat, but give practical demonstrations to rural people about easy preparation of wheat products.

CORRESPONDENCE

The Editor is not responsible for the views expressed by correspondents

Persistent Truncus Arteriosus

SIR,—I have read with great interest the above article of Dr. S. P. Khatua (*J. Indian M. A.*, **37** : 74, 1961) which is very informative. I must congratulate him for making the clinical diagnosis in this case, it being a rare congenital cardiac anomaly. The diagnosis can be confirmed only by cardiac catheterisation study and angiocardiography which shows the single trunk at the origin of aorta and pulmonary artery. This case of Dr. Khatua is an atypical case—"type IV" according to the classifications of Collett and Edwards (1949) as she had no pulmonary artery at all and instead there were two bronchial arteries providing the blood supply to the lungs. About this type of cases, we, the cardiologists, now-a-days think that "it may better be allocated both anatomically and clinically to the category of tetralogy of Fallot with pulmonary atresia" (Keith *et al*, 1958).

This case also had some uncommon features which deserve some comments, as for example,

(1) She was a child with cyanosis which is not so common in the 'usual' case of 'Persistent Truncus Arteriosus' unless associated with high pulmonary vascular resistance. Strangely enough, they usually have quite good arterial oxygen saturation (about 80 per cent) and pulmonary plethora.

(2) Postmortem examination showed gross right ventricular hypertrophy (also E.C.G. findings), which is only present in cases with high pulmonary vascular resistance.

In view of the total absence of the pulmonary artery it is difficult to diagnose this case as one with high pulmonary vascular resistance. I hope that Dr. Khatua will agree with my viewpoints that this case of his be better placed anatomically and clinically in the category of the "tetralogy of Fallot with pulmonary atresia". I am, etc.,

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REFERENCES

COLLETT, R. W. AND EDWARDS, J. E.—*S. Clin. North America*, **29** : 1245, 1949.

KEITH, D. J., ROWE, D. R. AND VLAD, P.—Heart Disease in Infancy and Childhood, The MacMillan Co., 1958.

Suicide and Barbiturates

SIR,—Your annotation on 'Suicide by barbiturates' (*J. Indian M. A.*, **37** : 193, 1961) has highlighted an important aspect of this problem, viz., the relatively easy access to the procurement of any barbiturate across the chemists' counter in this country. However, in spite of stricter regulations prevalent in the United Kingdom and elsewhere mortality statistics show that

there is a global increase in poisoning in general and with barbiturates in particular.

The conclusions drawn from cases of successful suicides do not always hold good for attempted suicides, but a study undertaken in this Institute on all successful suicides in Bangalore City has yielded interesting and informative data. All available particulars on suicides were extracted from police records maintained in the Central Police Office.

You have mentioned that within the short period of two weeks, three patients attempting suicide by barbiturates were encountered and they were all women. The analysis of our data shows that female suicide, by all methods, was more than male suicide over the three-year period 1958-1960 (9·1 to 8·4 per lakh of population). A similar but more prominent trend was observed in Saurashtra where the ratio of female to male suicide was 2 :1 over a four-year period (1952-55).

Comparison of the choice of method of suicide in Bangalore showed that among men hanging was employed by 25, 26·6 and 24 per cent in 1958, 1959 and 1960 respectively. From 1958 to 1960 there was a definite fall in cases of drowning from 47·7 per cent in 1958 to 22 per cent in 1960. 22·7 per cent employed poisoning (barbiturates and others) in 1958. It increased to 37·4 per cent in 1959 and 48·6 per cent in 1960—an increase of 26 per cent in poisoning from 1958 to 1960—a shift to the use of a more passive method. In women the methods employed for the years 1958, 1959 and 1960, in that order, were—hanging : 24·4, 20 and 9·5 per cent; drowning : 51·1, 45·3 and 46·1 per cent; poisoning : 14·3, 21·4 and 21·5 per cent. In Saurashtra suicide by burning accounted for 10 and 23·7 per cent of men and women respectively; it was negligible in men in Bangalore and accounted for 10·2, 21·4 and 12·4 per cent of female suicides in 1958, 1959 and 1960 respectively. In Saurashtra only 6 of 750 women and 35 of 279 men committed suicide by poisoning.

You have given prominence to socio-economic factors and 'lessened capability of tolerance' as causes for attempted suicides. Although we do not have figures for attempted suicides, in successful suicides in Bangalore, illnesses seem to play a major role in suicide. How far the illness contributes to the low socio-economic status or *vice versa* is a problem that needs further investigation. In Saurashtra, family tension was reported to be a major cause of suicide. Next in order were mental instability, prolonged illness, poverty and unemployment. It has been reported that illneases, both physical and mental, and social reasons are factors precipitating suicide in Japan. A high incidence of psychosomatic illnesses like peptic ulcer, cardiovascular illnesses, etc., has been found in suicides in the London area.

The remedy you have suggested, viz., stricter control of dispensing barbiturates can only be one measure for the prevention of suicides and at that not an important one. It is far more important that the general practitioner should have sufficient knowledge of the larval manifestations specially of depression and schizo-affective conditions and be able to pick out warning signs in the symptom-complex which need urgent psychiatric treatment. This approach will be far more rewarding than the one that you have suggested. I am, etc.,

All-India Institute
of Mental Health
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D. L. N. MURTI RAO
Director

REVIEWS

The Electrical Activity of the Nervous System—By Mary A. B. Brazier, PH.D., Second edition 1960, Pitman Medical Publishing Co. Ltd., London; 8½″ × 5½″, pp. 273; 35 sh.

Different chapters in this excellent monograph follow a pattern which is at once coherent and informative. Basic concepts of electrical changes associated with activity in the axon are dealt with commendable lucidity. Statements and reasons advanced about the electrical activity of more complicated structures of the nervous system have a clarity of their own. The book should be read by all interested in the fast-growing and fascinating subject of the electrical activity of the nervous system. Dr. Brazier should be complimented for her well documented and lucid presentation of the subject.

T. K. GHOSH

Relaxation for Childbirth—By Mary Barfield; 1960, William Heinemann Medical Books Ltd., London; 8″×5″, pp. 149; 12sh. 6d.

There is difference of opinion regarding the benefits of relaxation for childbirth. But those who practise it sincerely are well satisfied with its beneficial results.

Miss Barfield has dealt with the subject in a very practical manner by six lessons in a masterly way. She has also described the course and mechanism of normal labour in very simple language avoiding technical scientific terms as far as possible. Hence the book can be read and understood by non-medical persons.

The book will be of great value to obstetricians in general and to the expectant mothers.

S. SUR ROY

Antenatal and Postnatal Care—Edited by F. J. Browne, D.SC., M.D., F.R.C.S., F.R.C.O.G. and J. C. McClure Browne, B.SC., M.B., F.R.C.S., F.R.C.O.G.; 9th edition 1960, J. & A. Churchill Ltd., London; 9½″×6″, pp. 435; 45sh. net.

This well-known book edited by father and son continues to enjoy its popularity both among students and practitioners. Ever since its first publication it became a useful guide for theoretical considerations and practical approach to obstetrical problems. Lucid description of different facets of obstetrical complications made this book all the more interesting and attracted many readers.

Although the title of the book is Antenatal and Postnatal Care, it is mostly devoted to antenatal care. The authors have hardly done any justice to puerperium when it becomes abnormal and the methods to treat it.

The description of amenorrhoea and morning sickness as the signs of pregnancy is very confusing particularly to the undergraduate student. Printing mistakes add more to the confusion : to note the number of chromosomes in the female as 48 instead of 46 and the first of the three allelomorphic genes as Ce which should read as Cc. The chapters on pregnancy associated with some diseases maintain a high standard, particularly "Heart Disease in Pregnancy" which has been rewritten by Professor John McMichael. New conceptions and methods of treatment have been incorporated wherever applicable and their references are very useful. In spite of detailed description of treatment of diabetes in pregnancy, the role of oral antidiabetic drugs has not been mentioned. Discussions on its usefulness in the subsequent editions would be welcome. Professor J. Chassar Moir's excellent account on possibilities that might occur following x-ray exposure during pregnancy will act as a caution to radiologists and obstetricians.

The illustrations are plentiful and informative. The new size of the book is handy and the price is reasonable. The production is in conformity with the high standard maintained by the publishers.

S. Sur Roy

The Vagina, Annals of the New York Academy of Science, Volume 83, Art. 2—Consulting Editor—Warren R. Lang; 9″×6″, pp. 77-358; $4.00.

This monograph is the result of detailed work by reputed authors who made observations on different aspects of the vagina. The production is highly technical and its excellence will be appreciated very much by research workers who wish to solve its problems which are yet to be decided. Although the studies have been made from a wide angle, their usefulness to a clinician is limited. It will serve a useful purpose to a postgraduate student who wants to be conversant with up-to-date information on basic vaginal problems. The editor should be congratulated for this magnificent presentation.

S. Sur Roy

Transactions of the International Society of Plastic Surgeons, 2nd Congress, 1959, London—1960, E. & S. Livingstone Ltd., London and Edinburgh; 10″×7″, p. xxiv+589; 4.10s. net.

The momentum that plastic surgery has gained all over the world since the last world war is well reflected in this volume.

The transaction consists of a large number of papers presented in the 2nd Congress of the International Congress of the Plastic Surgeons held in London in 1959. The articles embrace almost all aspects of plastic surgery including the problem of homotransplantation of tissues.

The volume comprises of sixteen different sections, each containing a number of articles discussing different aspects of various problems of plastic surgery. The articles are profusely illustrated.

This transaction is indispensable for a person interested in plastic surgery as it gives a comprehensive idea about the problems faced by surgeons working under diverse circumstances all over the world. It also gives an idea about the recent advances that have been made in the field of plastic surgery and the line of thought of the modern workers which envisages the shape of things to come.

Anjali Mukherji

Health of the Community—By C. Fraser Brockington; 2nd Edition 1960, J. & A. Churchill Ltd., London; 8½″×5½″, pp. 345; 35sh. nett.

The second edition of this work is an indication of its favourable reception by the clientele for whom it was meant. Though primarily meant for the medical practitioners and students of medicine in U.K., especially in the context of the National Health Service now in operation there, this book is also of interest to the public administrators and the social welfare workers of various categories in other countries as well. With the widening horizons of the medical care programmes and with the provision of increasing health services for the community by the state, it is of importance to learn the factors that are associated with the organisation, function and utilisation of such programmes. National health services in any country to be effective and successful must be based on the core of preventive medicine, provision of treatment facilities can never meet the spiralling demands of curative services. Communities must be motivated to maintain their health, to promote health and to prevent diseases and disabilities in order to achieve optimum efficiency. The organisation, scope and function of a national health service in any country will depend on various factors of the socio-economic development of the country and pattern of social institutions evolved in a particular community.

In this book Professor Brockington very aptly and in an historical way discusses the evolution of the Health Services in England and the organisation and functions of the N.H.S. He rightly stresses that special techniques have to be evolved for community health practice as contrasted with the treatment on an individualistic basis. The vulnerable groups in the community need special study of their problems and the protection of these vulnerable groups requires collaborative efforts not only of medical practitioners and social workers but also of the people themselves. The education of people for health practice therefore assumes a very important place in community health programme. Professor Brockington has very rightly stressed on this aspect.

The role of hospitals, health centres, medical practitioners, and sanitarians has been adequately dealt with in the context of community health practice and utilisation of the available resources.

In India we are on the way to provide integrated (curative and preventive) health services through our community development programmes. The study of the community is therefore an essential pre-requisite to find out the nature and size of the health problems of a particular community before we can satisfactorily plan a comprehensive health service for the community.

Professor Brockington's book is valuable to interested workers in our country because of the scientific

methodology which he has adopted in the study of community health, basic principles of health services and future trends.

This book will be of help not only to the public health workers and health administrators, and students of medicine but also to other social welfare workers who are interested in the development of the community and the book is recommended for their study.

J. K. BHATTACHARYA

Everyday Prescriptions with Hints on Treatment –By Prankumar Guha, M.B., Major, I.M.S. (Retd.), 2nd edition (reprinted), 1961; published by the author, Calcutta. 4¼"×6½", pp. xviii+380; Rs. 7·00 net.

This little handbook outlines the treatment of common diseases met with in general practice, including some common disorders of the skin, eye and ear. It also contains special chapters on immunisation against common infectious diseases, blood transfusion, infusion of saline, acute poisoning, emergency drugs, insulins, pneumonia, and dietetics of the sick. The diseases have been arranged alphabetically for easy reference. It has an excellent bibliography, which is perhaps redundant in a book of this kind. This pocket size vade-mecum containing current practices in therapeutics can be confidently recommended to general practitioners. The book has a good format.

J. DHAR

OBITUARY

Dr. Banbehari Chaudhuri

Dr. Banbehari Chaudhuri was born on January 19, 1898 at Kasipur in Bankura (West Bengal). He matriculated in 1917.

In 1922 he passed the Final L.M.F. Examination from the Campbell Medical School securing the first place and obtained a gold medal for general proficiency. During his student career he was awarded seven silver medals. He was prosector in anatomy and class-assistant in all the subjects both in senior and junior classes.

DR. B. CHAUDHURI

He started his career as a private practitioner in the year 1922 at Bishnupur. He was an active member of the local I.M.A. branch, of which he was the President. His services as a medical practitioner were highly appreciated by the public. He was keenly associated with many religious and educational institutions.

Dr. Chaudhuri breathed his last on October 28, 1961 at the age of 63. He is survived by his widow, 3 sons, 4 daughters and innumerable friends and admirers.

YOUR QUESTIONS

Correspondents should give their names and addresses (not necessarily for publication) and include all relevant details for the questions which should be typed. Questions of medical interest will only be accepted for this section. They should be sent in a separate envelope marked "Your Questions". Questions of general interest will be published in preference. Lack of space precludes answering all the questions received.

ED.—*J. Indian M. A.*

Animal Inoculation in Diagnosis

Q. What is the position of animal inoculation in diagnosis in comparison with that of direct smear and cultural examination of the sputum?

Ans. The comparison of the three methods, viz., direct smear, culture and animal inoculation can only be relative. In actual practice repeated smears on three occasions from a 24 to 48 hours collection of sputum is the easiest and the best method. Cultural examination may enable the growth of the organisms in a few cases where smears have been negative. This method, however, takes a long time. Animal inoculation is mainly useful for toxicity tests. Its superiority is offset by the long duration of the experiment and availability of result.

A.T.S. and Tetanus

Q. 1. Is injection of A.T.S. necessary for a cut injury in a child aged 5 years, who had previously received A.T.S. injection at the age of 6 months?

2. Is it possible for a person to be attacked with fatal tetanus even when he had received A.T.S. injection within reasonable time after a cut injury?

Ans. 1. Yes, because A.T.S. gives passive immunity which lasts only for 3 weeks.

2. It depends on the dose of A.T.S. injected and the nature and surface area of the wound. In large unhealthy wounds the standard 1,500 unit dose is quite insufficient. A patient may develop tetanus due to large amount of toxin that is absorbed from a large surface area of the wound and he may die. But if a large amount of A.T.S. is injected then the ready-made passive immunity may help in preventing tetanus by neutralising the toxin.

If A.T.S. is injected immediately after the injury, it is quite all right. But if there is delay of a day or two, a much larger prophylactic dose is necessary.

The question of getting an attack of tetanus and death even after A.T.S. injection may be due to the following circumstances:

(a) When the potency of A.T.S. itself is questionable.

(b) When sufficient dosage of A.T.S. has not been administered.

(c) When the prophylactic dose of A.T.S. was not repeated when needed. In badly infected injuries A.T.S. has to be repeated almost every week until the wound has cleared up and A.T.S. is almost invariably needed if such wounds are operated for the second time.

SUPPLEMENT
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XXXVII ALL INDIA MEDICAL CONFERENCE, KANPUR, JANUARY 4-6, 1962

The organising secretaries of the 37th All India Medical Conference have issued the following :

Once again after 18 years Kanpur will be looking forward to the unique opportunity of opening its heart to receive our colleagues from every part of our great country as delegates and members of 37th All India Medical Conference which is being held at G. S. V. M. Medical College, Kanpur. The dates as notified earlier are :

Working Committee meetings : 29th, 30th & 31st December 1961.

Central Council meetings : 1st, 2nd & 3rd January 1962.

Conference on : 4th, 5th & 6th January 1962.

The Reception Committee is striving its best to make your stay at Kanpur as comfortable and pleasant as possible. For which purpose a Reception and an Enquiry Office is bieng opened at Kanpur Central Station on Platform No. 1, near the Railway Enquiry Office, where volunteers will receive you on your arrival and transport you and your luggage to the Delegates' Camp. For your convenience a list of connecting trains is being given below :

From Kashmere and Punjab via Saharanpur & Lucknow and from Assam via Lucknow

Lucknow Dep.	10-30	14-00	17-15	20-25	22-10	(N.E.R.)
Kanpur Arriv.	13-00	15-35	20-05	23-00	24-00	,,

Via Delhi

Delhi (Old) Dep.	...	...	...	8-45	21-40
Kanpur Arriv.	...	...	...	15-50	6-17

From Rajasthan & Gujarat via Agra & Toundla

Agra Fort Dep.	...	...	...	10-55	15-09
Kanpur Arriv.	...	...	...	15-50	19-50

From Maharashtra, Madras, Andhra, Mysore & Kerala via Jhansi

Jhansi Dep.	...	...	2-05	13-25	22-25
Kanpur Arriv.	...	...	8-40	17-50	4-35

From Orissa, Bengal & Bihar via Mougal Sarai

Mougal Sarai Dep.	...	...	1-40	7-19	12-20
Kanpur Arriv.	...	...	7-32	13-00	22-10

For those who want, staying arrangements have been made at the Conference Camp where beds and bed tea will be provided without charge. Special arrangements have been made for lady delegates and visitors coming with their families.

A Dining Pandal will be erected near the Conference venue which will start functioning from 29th December 1961, where breakfast, lunch, evening tea and dinners will be served against meal coupons. The charges for the same will be : Vegetarian :—Rs. 10/- per day; Non-vegetarian :—Rs. 12/- per day.

Children less than 10 years will be charged half rates.

Besides the Registration charges, there will be following charge for the Conference :

(a) Delegates :—Rs. 5/-; (b) Members of I.M.A. other than delegates :—Rs. 5/-; (c) Special Visitors :—Rs. 5/-; (d) Medical men who are not members of I.M.A. :—Rs. 10/-.

EXCURSIONS :

(a) Kanpur has a hoary past with an important historical background. Besides it is a great industrial and trading centre manufacturing aeroplanes, military stores and woollen, cotton, rayon, jute, leather, iron, plastic, surgical and pharmaceutical goods. Interesting places inside the city are Allen Forest, Kamla Retreat, Kamla Mandir, Moti Jheel, Sarsaiya Ghat, Tantiya Tope Park Ganesh Udyan, Nehru Bagh, Nana Rao (Satti-chaura) Ghat, Jajmau, Glass Temple, J. K. Rayon Mills and Medical College. To give you a glimpse of Kanpur, the Reception Committee is arranging a visit to these places free of charge, starting from the Medical College and back again there every day.

(b) Bithoor also known as Bramhavart, where Brahma offered worship after creating the universe is a religious and historical place, 12 miles from Kanpur. It is famous for the War of Independence of 1857 and is connected with the famous names of Rani of Jhansi, Tantiya Tope and Nana Saheb. At this very place the armies of Rama were defeated by Lava and Kush and great epic of Ramayana was written by Valmiki. Buses will daily leave for Bithoor on 2nd, 3rd, 5th and 6th January 1962 and a nominal charge of Rs. 2/- will be charged per head.

(c) Lucknow : 50 miles from Kanpur on the southern bank of river Gomti is known as the City of Gardens and Palaces and is famous for its culture and historical past. It is the capital of Uttar Pradesh. Its oriental grandeur is even today deposited in its old buildings like the Imambaras, Sikandar Bagh, Dilkusha, Residency etc. Other places worth visiting are Museum, Zoo, Medical College, etc. Bus trips will be arranged for Lucknow on 3rd, 5th and 6th January 1962, from 12 noon and return at 8 P.M. The charges will be Rs. 10/- per head and for children will be Rs. 5/-.

(d) Khajuraho : It is nearly 127 miles from Kanpur in Madhya Pradesh. A place of ancient civilisation built by Chandel as their capital, it still abounds in ageless grandeur of temples which abound in rare combination of religious emotions with artistic genius of the highest order. The temples are full of carvings and decorations of gods and godesses of the highest artistic value. A trip to Khajuraho is being arranged on the 2nd and 5th January 1962. It requires a night's halt at the rest house, which needs booking well in advance. The trip will cost Rs. 30/- per adult and Rs. 10/- per child above 7 years of age. Further information and details about excursion, may be had from the Organising Secretary Dr. Navin Chandra or Convener Dr. R. N. Sen, Aryanagar, Kanpur.

While promising that no effort will be spared to make you feel absolutely at home, it is requested that

members may kindly fill in the following form, and send it at an early date so that proper arrangements may be made well in time to avoid any inconvenience to you."

This form must reach the Organising Secretaries, 37th All India Medical Conference, "Temple of Service", Mahatma Gandhi Marg, Kanpur, before 15th December 1961.

I wish to attend the 37th All India Medical Conference, Kanpur as Member w.c./Member c.c./Delegate/Member/Visitor from.....
Branch.....state.....

I will arrive at Kanpur by.....train on.....and return by.....train on.....

Please arrange my return journey to.....
for.....males.....females.....children.....
from Kanpur by.....train on.....1962
.....Class Ticket No.....

* * * *

Name Block letter..... Registration No.....
Branch.....
State.....

Please make arrangements for my stay at.....
Hotel/Delegates camp from.....to.....
both days inclusive. M.O./Bank Draft on.....
Bank, Kanpur for Rs.....enclosed herewith
.....males.....females.....children

* * * *

Name..... Registration No.....
Branch.....
State.....

Please make arrangements for my board at the Dining Pandal from.....to.....
Males.....Females.....Children.....

I want non-vegetarian/vegetarian meals.

* * * *

Name..... Registration No.....
Branch.....
State.....

I will join the trip to (a) Bithoor (b) Lucknow (c) Khajuraho. Please issue tickets for.....adults .....children. I am sending Rs..... as full payment for the same.

Signature.....
Name in block letters
Dr.....
.....
Address.....

Strike out which is not necessary.

BRANCH NOTES

ALLEPPEY BRANCH—The annual report of the branch for 1960-61 shows that 12 meetings were held during the year and interesting lectures on clinical subjects were arranged. The following are the office-bearers for 1961-62: President—Dr. S. V. Subramanya Iyer; Vice-President—Dr. K. Y. Roy; Representative to State Council—Dr. Jacob Thomas; Representative to the Central Council—Dr. K. Kuruvilla; Treasurer—Dr. P. N. Kumaran Nair; Jt. Secretary—Dr. Ignatius; Hony. Secretary—Dr. K. N. Pillai.

AURANGABAD BRANCH—The annual general meeting of this branch was held on 8-10-61 at the residence of Dr. T. P. Sinha and the following members were elected office-bearers for the year 1961-62.

Dr. D. Jha—President; Dr. H. B. Sahay and Dr. A. K. Bose—Vice-Presidents; Dr. A. K. Mitra—Hony. Secretary; Dr. B. Singh—Jt. Secretary; Dr. L. P. Sinha—Treasurer; Dr. B. Prasad—Auditor; Dr. D. D. Prasad—Representative to Central Council; Dr. A. K. Mitra and Dr. T. P. Sinha—Representatives to State Council.

BAHRAICH BRANCH—The monthly meeting of the branch was held in the office of Civil Surgeon with Dr. R. P. Dhawan in the chair. Minutes of last meeting were read and confirmed. Meetings of the branch were held regularly and the membership increased to 35.

The annual election of office-bearers was held and Dr. R. P. Dhawan was re-elected as President.

A resolution for having a building for the branch was passed. A few interesting cases were demonstrated and Dr. J. B. Singh, Leprosy Medical Officer read his paper on Leprosy.

BAREILLY BRANCH—The annual general meeting of the branch was held on the 25th September 1961 at 8-30 P.M. in the District Hospital out-patient department. Fifty members were present.

Before going through with the agenda an appeal to the local members was made to attend the U. P. State Medical Conference in good number and get their enrolment to the Reception Committee membership at an early date. The members were acquainted with information regarding the World Medical Association Conference due to be held.

Dr. M. K. Goel, the honorary secretary read out his report for the working of the association for the year 1960-61.

Election of the office-bearers and the executive committee was held. The following were elected:

President—Dr. C. M. Aga; Vice-Presidents—Dr. A. D. Bhandari (sr.) and Dr. P. C. Bhalla (jr.); Hony. Secretary—Dr. M. K. Goel; Treasurer—Dr. J. S. Garg; Representative, Hospital Advisory Committee—Dr. A. B. L. Mathur; Association Auditors—Dr. S. Zahid Ali and G. S. Dhillon.

A meeting (clinical) of the branch was held on the 15-9-61. About fifty members attended the same. Dr. S. C. Pal, Surgical Specialist to the District Hospital was the speaker of the day the subject being "Acute Appendicitis and its Management". This was followed by some case demonstration of clinical interest.

An executive committee meeting was held on 20-9-61 at Dr. C. M. Aga's residence. 17 members were present. Dr. C. M. Aga who presided read out the secretary's report about the representation to the Chief Minister regarding the recognition of the B.M.B.S. course. The minutes of the last executive committee meeting were read. Forthcoming U.P. State Medical Conference was discussed and an appeal to the members was made to enrol themselves as the members of the reception committee for the same.

A general review of the accounts for the year 1960-61 was made and it was decided to appoint M/s. R. C. Tandon & Co., Chartered Accountants for the Association.

Annual General Meeting of the Branch due to be held in the third week of the month was discussed about and a review of the prospective candidates for the election was made.

A clinical meeting of the branch was held on the 21-9-61 at the N.E. Railway Hospital, Izatnagar, Bareilly. Dr. S. N. Ray of the Railway Hospital was the speaker, the subject being Liver Abscess. The meeting was attended by forty-two members. The speaker speaking for about an hour discussed the subject very thoroughly.

BARSI BRARNCH—The following have been elected office-bearers of the branch for 1961-62: President—Dr. M. G. Nane; Vice-Prresident—Dr. (Miss) S. S. Karpe; Hony. Secretary—Dr. M. B. Talegaonkar and Hony. Treasurer:—Dr. D. G. Kasyapi.

BHIWANDI BRANCH—A monthly meeting of the branch was held on 5-10-61. 9 members out of 12 attended the meeting. Dr. A. G. Desai and Dr. Bhalchandra Medhekar attended the meeting. Dr. A. G. Desai gave a talk on convulsion in infants. Dr. S. K. Acharya presided.

BHOPAL BRANCH—The annual meeting of the branch was held on 30-10-61 in the Lecture Hall of Hamidia Hospital, Bhopal under the presidentship of Dr. R. P. Bhargava. Hony. Secretary, Dr. R. K. Bhargava, read the annual report, and Hony. Treasurer, Dr. S. N. Sen Gupta, presented the audited accounts for the year 1960-61.

Elections this year also, like the previous year, were unanimous and the results are as follows :

President—Dr. M. Kumar; Vice-President—Dr. Ajai Shanker; Secreary—Dr. R. K. Bhargava; Jt. Secretary—Dr. Zahirul Islam; Hony. Treasurer—Dr. N. P. Misra.

The annual report of the branch for 1960-61 shows that 7 clinical meetings, 1 ordinary meeting, 2 meetings of the executive committee were held during the year. In the clinical meetings original papers were read and cases of clinical interest were presented. The president and secretary launched membership drive and membership increased from 47 to 89. The notable achievement of the year was the functioning of the voluntary rural medical relief centre at Misrod village. The work taken up there was both preventive and curative. Though it was planned to start a second centre, it could not be taken up because of conveyance problems. World Health Day was celebrated, and the president addressed a well attended meeting.

BISHNUPUR BRANCH —The members placed on record on 29-10-61 deep sense of sorrow at the sudden death of the president, Dr. Banbehari Chowdhury and observed condolence by standing in silence for one minute and tendered their deep sympathy to the members of the family of the departed.

CHETTINAD BRANCH —At the tenth annual meeting of the branch the following office-bearers for the year 1961-62 were elected on October 28, 1961 in the Alagappa Training College Hall, College Campus, Karaikudi.

President—Dr. S. Subramaniam; Vice-President—Dr. A. Vaidyanathan; Hony. Secretary—Dr. (Capt.) G. D. Ebenezer; Jt. Secretary—Dr. P. K. Narayanan; Treasurer—Dr. A. Rahman; Representative to the Provincial Council—Dr. M. Srinivasalu; Representative to the Central Council—Dr. A. Rahman; Auditor—Dr. A. Vaidyanathan.

On October 28, 1961 after the election of office-bearers a combined Medical Conference of Madurai and Chettinad Medical Associations was held in the Alagappa Training College Hall, College Campus, Karaikudi at 5 P.M. The following speakers addressed the meeting : Dr. G. C. Anbunathan, Hony. Physician, Government Erskine Hospital, Madurai on Vomiting—Significance and Management; Dr. K. Bhaskara Rao, Professor of Obstetrics and Gynaecology, Madurai Medical College on Some Obstetrical Problems; Dr. K. A. Ramalingam, Government Erskine Hospital, Madurai on Some Common Orthopaedic Problems.

At the monthly meeting of the branch held on 30-10-61 in the S.M.S. High School, Karaikudi, the members placed on record their deep concern over the recent proposal of the Health Minister of Madras State to produce semi-doctors. It was felt unanimously that the Indian Medical Association in particular and the medical profession in general should strongly protest against this move and request the State Government to reconsider the matter.

CHHATARPUR BRANCH —The doctors of Chhatarpur in a meeting held on 5-10-61 opened a branch at Chhatarpur from 1-10-61. The following office-bearers were elected unanimously : President—Dr. R. N. Shrivastava; Secretary—Dr. S. P. Chatterjee; Treasurer—Dr. B. M. Pathak.

DURGAPUR BRANCH —The annual general meeting was held on September 24, 1961 with 20 members present. The proceedings of the last meeting were confirmed. The following were elected office-bearers for 1961-62 :

Dr. Basanta Kumar Chatterjee—President; Dr. N. K. Guha Neogi—Vice-President; Dr. Manindra Nath Das Gupta—Hony. General Secretary; Dr. Salil Mitra, Dr. M. K. Goswami and Dr. (Capt.) S. C. Lahiri—Jt. General Secretaries; Dr. P. N. Mukherjee—Hony. Treasurer; Dr. Manindra Nath Das Gupta or Dr. A. K. Ghosh as member of the Central Council and Dr. Manindra Nath Das Gupta and Dr. Salil Mitra were elected members of the Provincial Council.

GADAG BRANCH—The annual general body meeting was held on October 14, 1961. Dr. G. S. Kulkarni presided. The following office-bearers were elected for the year 1961-62 : President—Dr. G. S. Kulkarni; Hony. Secretary—Dr. M. R. Patil; Hony. Jt. Secretary—Dr. R. A. Jalihal; Hony. Treasurer—Dr. B. J. Athawale; Hony. Auditor—Dr. A. V. Umachigi; Central Council Representative—Dr. R. R. Joshi; State Council Representative —Dr. G. S. Kulkarni.

Earlier Dr. M. R. Patil, the secretary read a report of last year's activities of the branch. There were 22 members on the roll, 12 monthly meetings were held. The following papers were read and cases of interest shown : (a) Dr. R. A. Jalihal read papers on Recent finding on Amoebiasis and Non-cardiac Congestive Failure; (b) Dr. R. A. Jalihal demonstrated a case of Fibrosis of Lung in a Young Boy, a case of unusual Vascular Disease, X-ray findings in Pott's Disease; (c) Dr. G. S. Kulkarni gave information on The Present Position of Corneal Graft.

There were two distinguished visitors to the branch, (a) Dr. Roy, Director, National Malaria Eradication Programme, New Delhi visited the branch on 13-6-61. He explained the objects and methods of the programme. (b) Dr. B. V. Mulay, Sholapur, ex-president, I.M.A. met the members of the branch on 3-9-61. He gave a talk on Recent Trends in Medical Treatment.

The branch observed 'Anti-Leprosy Day' on 30-1-61 and World Health Day on 7-4-61 by arranging suitable lectures.

JALGAON BRANCH—The annual meeting of the branch was held on October 8, 1961 at Paldhi. The following office-bearers were elected : President—Dr. Miss Yashodabai Choudhary; Vice-President—Dr. S. V. Sahasrabudhe; Hony. General Secretary—Dr. K. B. Patil; Jt. Hony. Secretary—Dr. P. M. Choudhary; Representative to the Central Council—Dr. S. D. Athawale; Representatives to Maharashtra Territorial Council—Dr. K. B. Patil, Dr. D. R. Kulkarni and Dr. S. S. Mhalas.

JAMNAGAR BRANCH—The annual general dinner meeting of the branch was held on 24-9-61 at Shri M. P. Shah Medical College Hostel no. 6 at 8-45 P.M. Dr. M. V. Rajapurkar was in the chair. Dr. T. B. Patel, Director of Health and Medical Services, Government of Gujarat was the Chief Guest. Dr. N. R. Desai, Dean, Civil Hospital, Ahmedabad was also invited. 57 members and 10 guests were present.

The meeting began with a prayer. The Oath of Maimonides was read by Dr. V. S. Chudasama and the House heard it standing.

Minutes of the last meeting having been passed, Dr. S. S. Baxi introduced the Chief Guest, Dr. T. B. Patel and Dr. N. R. Desai. Dr. M. V. Rajapurkar then welcomed the chief guest, garlanded him and delivered his presidential speech. In his presidential address, Dr. M. V. Rajapurkar said *inter alia* : "I have observed both in our country and abroad, that the general practitioner is developing an inferiority complex and feeling of being relegated to the background. I wish to state with all emphasis that every effort should be made to dispel this feeling. Going over a series of discussion I can state that nearly every one believes that good general practice is still essential for any medical service." He quoted Prof. Hunt, Prof. Silver and Dr. Fox, editor of *Lancet* in his support. Dr. Rajapurkar said "far from being relegated to the background the practitioner, is as important today as ever before, probably more so. His responsibility has however increased under the pressures of changing social situations and changing medical knowledge."

"Since 'Service to the Sick' is our sacred heritage and our prime responsibility, it behoves us to keep uptodate by continuous contact with changing and advancing medical knowledge for it is then only that we can render valuable and correct service to the sick and give an opinion that would be respected."

Next he emphasised on the unity in the profession, and to ensure this unity doctors should join the I.M.A. in large numbers. He referred to research in his address and said, "First class research does not necessarily need very advanced laboratories with uptodate equipment. More than anything it needs a very observant eye. I may remind you that many researches which are classic by any standard have come from practitioners and from places, which had no laboratories by modern standards. To take a few examples the use of glycerinated thyroid extract in treating myxoedema, the use of ephedrine in asthma, the discovery and effects of adrenaline on circulation, the gift of digitalis to the medical profession, the preventive value of vaccination and a host of other magnificent contributions have come from observant practitioners.

"I therefore urge every one of us to be more vigilant and observant and a chance may come our way of making a solid contribution to lessening of human suffering. I could not ask for more. I have here, particularly in mind, the entity of 'predisease state', to the study of which the practitioner has a splendid opportunity." He also discussed prevention of diseases, and said "We have reason to be specially proud because of the great heritage of preventive thought of Ayurvedic medicine. It is our responsibility to advise the nation, our fellow countrymen and patients on the prevention of disease and on the preservation and promotion of health. The results of sound and vigorous development of Preventive and Social Medicine should be apparent."

Next the Annual Report of the Association was presented by Hony. Secretary, Dr. H. L. Patel. Main points in the report : 1. Rise of membership to a peak of 74, total 18 meetings; 2. Formation of Constitution sub-committee and passing the amended constitution; 3. Nine clinical meetings held, 43 cases shown; 4. Contribution of over Rs. 1,100 to Rajkot Conference by our members; 5. Two film shows; 6. A symposium, a trip to Sikka, 3 dinner meetings, 2 business meetings and a condolence meetings; 7. Considerable improvement in attendance at meetings; 8. School health work, 1,849 children examined.

In absence of the Treasurer, Dr. Nansey, the annual accounts were read by Dr. H. L. Patel.

The results of election of office-bearers were next announced. The following were declared elected uncontested : President—Dr. V. S. Chudasama; Vice-President—Dr. V. P. Bhatt; Jt. Hony. Secretaries—Dr. H. L. Patel and Dr. R. L. Vadi; Hony. Treasurer—H. J. Nansey.

The president, then, welcomed the president-elect, Dr. Chudasama, who gave a short speech, in which he thanked the house for electing him to this high office. The Chief Guest, Dr. T. B. Patel, Director of Health and Medical Services of the State then gave a speech emphasising preventive and social aspects of medicine specially in respect of diseases like tuberculosis.

KANDI BRANCH -At the annual meeting of the branch the following were elected office-bearers for 1961-62 : Dr. B. Chakravorty—President; Drs. R. Mondal and K. Chatterjee—Vice-Presidents; Dr. S. Ghosh—Secretary; and Drs. P. Shaha and A. Paul—Joint Secretaries. Outgoing secretary Dr. S. Ghosh placed the annual report and audited accounts. The branch has organised a library with books and journals received from the British Medical Association and other sources. Members took part in T. B. Seal Sale. A milk canteen catering free milk to 250 children daily has been opened at Kandra under Khargram P.S. Milk powder was received as a donation from the people of America through the UNICEF. At clinical meetings of the branch Drs. S. Mukherjee, S. Das Gupta, R. Acharya, B. Trivedi and P. Nag respectively read papers on Acute Abdomen and its Management, Eye strain and visual hygiene, Public Health report of the district of Murshidabad, Experiences in Ghana, West Africa and Cardiovascular Emergencies in General Practice. The meeting adopted a resolution demanding immediate electrification of G. C. Hospital, Kandi and Health Centres at Panchthupi, Gokarna and Bahara.

KANPUR BRANCH—A clinical meeting was addressed by Dr. O. P. Mittal, who has come back recently from Continental Educational Tour under Colombo Plan on Radiological Differential Diagnosis of Pulmonary Tuberculosis on 25-10-61 at 4-30 at the "Temple of Service". Dr. Satwant Singh presided.

KARIMNAGAR BRANCH—The monthly clinical meeting of the branch was held on October 1, 1961 at the Primary Health Centre, Kothapalli, under the presidentship of Dr. Ahmed Hussain, Superintendent and D.M.O., Karimnager. The Hony. Secretary read some notifications issued by the Central office, and it was unanimously agreed to depute Dr. Nagabooshanam, to represent the branch at the annual meeting of the Indian Medical Association to be held at Kanpur. Dr. G. Surendra Mohan Rao, Malaria officer, appealed to the members to co-operate with his department, in the plan schemes of Eradication of Malaria. Dr. Hanumantha Rajam, Assistant Surgeon, District Headquarters Hospital, Karimnagar, presented forty-two cases of Tetanus that are being treated at the Headquarters Hospital, and briefly described the aetiology, signs and symptoms, pathogenesis and the line of treatment that is followed at the Headquarters Hospital, Karimnagar, which is giving encouraging results. Dr. Habeeb-ur-Rasool presented a case of Pneumonia with Jaundice who responded very well with treatment, along with x-rays.

Dr. Ahmed Hussain, Superintendent and D.M.O., Karimnagar, presented a series of cases of Ascites who were progressing very well with "Intravenous Vitamin B_6, B_{12}, and other routine drugs that are given for Cirrhosis Liver."

KATHOR BRANCH—The annual meeting of the branch was held on 17-9-61; and following office-bearers were elected for the year 1961-62 : Dr. V. N. Vaishanav—President; Dr. N. N. Chauhan—Vice-President and Dr. G. K. Thakor—Secretary.

The annual report shows that it has the strength of nine members. There were two clinical meetings. In the last meeting the subject "Allergy" was discussed. Dr. N. N. Chauhan, Dr. G. K. Thakor, Dr. R. M. Patel took part in the discussion and stated their experiences regarding allergy.

KATIHAR BRANCH—Since conditions of the Medical Officers in the Bihar State are poor and have deteriorated, presently the medical profession is considered less attractive than most other professions and services in the State due to inadequate pay scales, the branch strongly endorsed the recommendations of State Medical Association regarding the revision of pay scales and reorganisation of services.

The members of the branch felt a deep concern at the havoc created by the recent flood in Bihar State especially in the district of Monghyr. The members would be glad to render their services, if requisitioned by the Bihar State. In the meantime each member was requested to contribute at least Rs. 5/- to the Bihar Flood Relief Fund immediately.

K. G. F. BRANCH—The monthly clinical meeting was held on 20-10-61 at Civil Hospital. 15 members were present. Dr. B. N. Krishnamurthy presided over the meeting. Dr. K. Kulasegaran presented a case of T. B. abdomen, Dr. B. S. Veerabhadrappa presented a case of Hydronephrosis, Dr. M. Punyamurthy demonstrated a case of Osteogenic Sarcoma left thigh. Dr. B. N. Krishnamurthy demonstrated a case of Eosinophilic Lung. After a lively discussion the meeting came to a close.

MALEGAON BRANCH—The annual meeting of the branch was held on September 24, 1961 at 6-0 P.M. at the residence of Dr. P. M. Rehmany. Proceedings of the last two meetings were read and confirmed. Letters and circulars received were discussed. The Auditor's report for the last year 1960-61 was accepted. The annual report and the statement of accounts of the last year were approved. The report of the working of the Triple Toxoid Injection Centre and the statement of the account of same were approved. Provisional budget for the next year 1961-62 was sanctioned.

The following members were elected as office-bearers for 1961-62: President—Dr. Khaleel M. Ansari; Vice-President—Dr. R. N. Bendale; Hony. General Secretary—Dr. G. S. Parnaik; Jt. Hony. Secretary—Dr. N. B. Shah; Auditor—Dr. B. V. Hiray; Representative on the Central Council—Dr. N. B. Shah; Representative on Provincial Council—Dr. R. B. Bhandari.

MORADABAD BRANCH—The twenty-seventh annual meeting of the branch was held on October 1, 1961 at 7-30 P.M. at the Senior Railway Institute with Dr. Hans Raj in the chair. The Hony. Secretary Dr. V. P. Rastogi presented the annual report for the year 1960-61 which was read and signed by the President. The special feature of this year was the invitation extended to the wives of the doctors to attend the meeting, which they attended in large numbers. It was a social and colourful gathering, non-members from the city and adjoining places were also invited. The attendance was more than a hundred. The following elections were held, and the members only participated: President—Dr. Hans Raj; Vice-President—Dr. J. S. Rastogi; Hony. Secretary—Dr. V. P. Rastogi; Joint Secretary—Dr. R. D. Gupta; Treasurer—Dr. G. Mujtaba; Members of Central Council—Dr. J. S. Rastogi; Members of State Council—Dr. J. S. Agrawal and Dr. P. N. Trivedi.

The annual report of the branch for 1960-61 shows that membership increased by 7. Many clinical lectures were arranged during the year. The activities of the branch were manysided.

A short cultural programme comprising of dances, songs, and kawalies was displayed. Dr. H. S. Pant gave a very interesting caricature of the medicine seller in the street, and Dr. Harnam Singh gave a joke, which was enjoyed by all.

MUZAFFARNAGAR BRANCH—Twelve ordinary meetings were arranged in 1960-61 besides one emergency meeting and one Symposium on Tuberculosis and its various manifestations. In the monthly meetings Drs. S. B. Bhargava, Hira Lal, J. S. Singhal, Rajendra Singh, K. S. Chuga and K. N. Singh spoke on 6 different medical subjects including Rheumatic Fever, Coronary Thrombosis, Coma, Contraception, Levers, Malaria Eradication. Five film shows were arranged in which 9 films on medical subjects were shown.

One meeting was arranged in Jansath and the trip by cars proved a happy change.

Five new members were enlisted. 274 students were examinned by the members of the branch who donated their valuable time.

The branch took lead in passing the protest resolution against recognition of B.M.B.S. degree by the U. P. Medical Council and their being made eligible to join the P.M.S. II cadre of U. P. State Government. The branch invited State Branch to hold the U. P. State Conference next year in Muzaffarnagar.

MYSORE BRANCH—The annual general meeting was held on September 30, 1961. Dr. H. V. Suryanarayan Rao presided. 17 members were present. The Hony. Secretary read the report for the year 1960-61. The audited account was presented and passed. The budget for the ensuing year was passed.

The following members were elected as office-bearers of the branch for the year 1961-62: President—Dr. V. Ramachandra Naidu; Vice-President—Dr. Y. P. Rudrappa; Hony. Secretary—Dr. Anandi Bai Prasad; Hony. Jt. Secretary—Dr. R. Narayanaswamy Setty; State Council Members—Dr. K. Basappa, Dr. M. V. Jayamma, Dr. R. Seshadri Iyengar, Dr. P. R. Satyanarayana Setty; Central Council Members—Dr. H. V. Suryanarayana Rao, Dr. Anandi Bai Prasad; Internal Auditor—Dr. D. Srinivasa Murthy; External Auditor—Sri H. S. Venkata Rao.

It was resolved that "In view of the introduction of prohibition in Mysore the Government may be approached for the issue of permits for alcohol for all members of the Indian Medical Association for medicinal purposes."

NAGAUR BRANCH—A meeting of the branch was held at Jaswantgarh on 17-9-61 with Dr. M. L. Sharma, D. M. & H.O., Nagaur in the chair. 16 doctors attended the meeting.

Circular letters received from the central office and provincial branch of I.M.A. were read to the members.

Discussions were held on "Kwashiorkor". Dr. G. M. Mathur and Dr. A. H. Qureshi spoke on the aetiology, pathology, clinical picture, treatment and preventive measures of Kwashiorkor. Dr. Krishna Kumar and Dr. K. D. Shama also took part in the discussions. It was decided to have discussions on the Management of Acute Abdomen in the next meeting.

The House then considered the Rajasthan Government's order abolishing C.A.S. I and C.A.S. II and making it one cadre C.A.S. The house welcomed the decision of the Government but expressed concern at the plight of the licentiates who will stop at Rs. 400/- in the scale of Rs. 200-700 according to the new circular. Previously the licentiates had some chances of promotion to C.A.S. I cadre after certain period of service. This opportunity to the licentiates has been denied by the new circular. The House decided unanimously to request the department and the I.M.A. to take up the matter with the Government to waive this condition and allow the licentiates a fair chance to reach the maximum of the pay scale.

Election of office-bearers for the year 1961-62 was also held. The following were unanimously elected: Dr. M.

L. Sharma—President Dr. Devi Singh Rathore—Vice-President; Dr. G. M. Mathur—Hony. Secretary-*cum*-Treasurer.

A meeting of the branch was held at Nagaur on 28-10-61.

In the opinion of the members the restriction imposed by the Rajasthan Government for the licentiates to stop at Rs. 400/- in the scale of Rs. 200-700 be waived off as in previous pay scale the licentiates were eligible for promotion to C.A.S. I in the pay scale of Rs. 250-700 after 15 years' service and this opportunity has been denied to them in this new amalgamated pay scale.

The doctors also expressed concern that the medical examination of students in this district is conducted by quacks or Ayurvedic practitioners. They have requested the D.M.H.O. Nagaur to take up the matter with the higher authorities so that qualified doctors conduct the medical examination.

A talk on "Management of Acute Abdomen" was given by Dr. Mahendra Singh. He discussed the causes and management of Acute Abdomen. Dr. M. L. Sharma narrated his own experiences and cited two cases attended by him at Pali. Drs. K. D. Sharma and Devi Singh Rathore also took part in the discussions.

NASIK BRANCH—The following is a list of office-bearers of the branch for 1961-62: President—Dr. L. H. Patil; Vice-President—Dr. M. K. Damle; Hony. Secretary and Treasurer—Dr. S. K. Kirloskar; Provincial Council members—Dr. D. V. Kulkarni, Dr. H. S. Joshi, Dr. T. V. Mhaskar, Dr. A. S. Chitko and Dr. R. K. Goyadhani; Central Council member—Dr. D. V. Deolalkar.

The annual report of the branch for 1960-61 shows that 5 new members were enlisted. The 3rd Maharashtra Territorial Medical Conference was held at Nasik during the year. The B.C.G. campaign was carried out. 1520 Triple Vaccine injections were given at the Triple Vaccine Centre. The Family Planning Centre showed steady progress. The library was revived and a Children's Health Insurance scheme was introduced.

NORTH MALABAR BRANCH—The IX Annual General Body Meeting of the branch was held on October 8, 1961, at Cannanore, with the President, Dr. P. K. Narayanan, in the chair. The Hony. Secretary, Dr. Mohamed Husain, presented the annual report. The following were elected as office-bearers: President—Dr. P. K. Narayanan; Vice-Presidents—Dr. Miss K. P. Novaky, Dr. M. Mohamed; Hony. Secretary—Dr. V. Mohamed Husain; Hony. Jt. Secretary and Treasurer—Dr. P. V. Karunakaran Nair; Representative to the Central Council—Dr. K. P. Ramakrishnan; Representatives to the State Council—Dr. R. F. Peters, Dr. M. Mohamed. An Executive Committee of six were also elected.

Lt. Col. G. R. Parasuram, President of the Kerala State Branch, of the I.M.A. spoke on the organisation of the I.M.A. and the importance of increasing the membership.

In the scientific session, Dr. C. K. Ramachandran spoke on "Uses of Anticoagulants in Medical Practice" and Dr. Matthew John on "Anaemias and General Surgery".

PALGHAT BRANCH—The annual report of the branch for the year 1-10-60—30-9-61, shows an increase in membership. This branch have nearly 100 per cent of representation of practitioners in modern medicine in the district. Five meetings of the executive committee, 5 of the general body, 4 lecture meetings and a farewell function in honour of Dr. V. S. Gopalakrishnan, on the eve of his transfer, were held during the year. The branch had the privilege of holding the 4th Kerala State Medical Conference.

PORBANDAR BRANCH—The general meeting of the branch was held on 8-10-61 at 6-30 P.M. in Villa No. 2 Seashore Willingdon Marina, Porbandar. Dr. H. H. Chavda was in the chair.

Twentytwo members were present.

The following office-bearers for 1961-62 were elected: President—Dr. H. H. Chavda; Vice-President—Dr. B. N. Joshi; Hony. Secretary—Dr. B. D. Jhala; Hony. Joint Secretary—Dr. R. A. Lakhani; Hony. Treasurer—Dr. R. N. Maru; Central Council member—Dr. P. B. Pandya. Dr. C. R. Shah was elected as the member of the Advisory Board of the Bhavsinhji Hospital. The statement of accounts for the year 1960-61 was noted. The annual report of the branch for 1960-61 shows that membership has gone up from 20 to 26. Four meetings were held during the year of which 2 were clinical meetings. Dr. Chavda and Dr. Jhala carried out the medical examination of the students without any remuneration and six members gave the Triple Antigen injections to 7,000 children.

SHAMLI BRANCH—An emergent meeting of the branch was held at the residence of Dr. B. L. Sharma to consider a letter sent by a representative of the students of the Vaish Degree College, Shamli, requesting this Association to look after the health of the students who have started hunger strike.

After due consideration this committee decided to look after the health of these hunger-strikers, though the Committee did not like the action taken by the students.

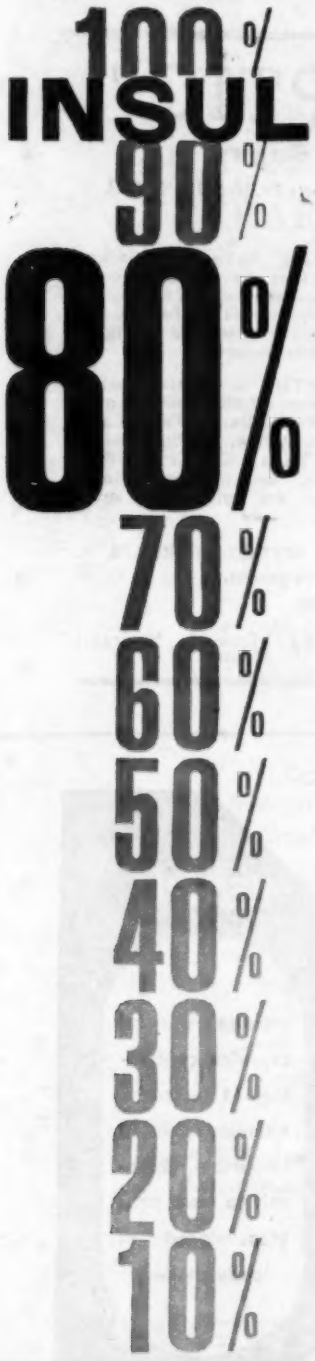
TIRUCHY BRANCH—List of office-bearers elected at the 32nd annual general body meeting held on October 29, 1961 in the Medical Association Building, Salai Road, Tiruchy.

President—Dr. T. V. Ranganathan; Vice-President—Dr. C. R. Chary; Secretary (re-elected)—Dr. N. V. Muthukrishnan; Joint Secretary and Treasurer (re-elected)—Dr. M. V. A. Iswaran; Representatives to the State Council—Dr. A. Dharmarajan, Dr. N. C. Subramanyam, Dr. V. K. Ranganathan, Dr. V. Enok and Dr. S. Venkatesan; Representatives to the Central Council—Dr. T. V. Srinivasan and Dr. V. K. Ranganathan.

XVI MADRAS STATE MEDICAL CONFERENCE, 1961, VELLORE

The 16th Madras State Medical Conference will be held under the auspices of the North Arcot Branch of the Indian Medical Association on the 22nd and 23rd of December 1961 at the Christian Medical College campus, Vellore, North Arcot district. A Reception Committee has been formed with Dr. J. S. Carman, Director of the Christian Medical College, Vellore, as Chairman, and Dr. T. M. Kumaraswami as the Organising Secretary. A very interesting scientific session is being organised, and eminent members from the faculty of the Christian Medical College, Vellore, will take part in the deliberations. A Souvenir will also be brought out to commemorate the occasion.

Members requiring any information pertaining to the conference are requested to kindly contact Dr. T. M. Kumaraswami, Organising Secretary, 16th Madras State Medical Conference, 32, Thennamaram Street, Vellore, N. Arcot district.



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